THE LANCET

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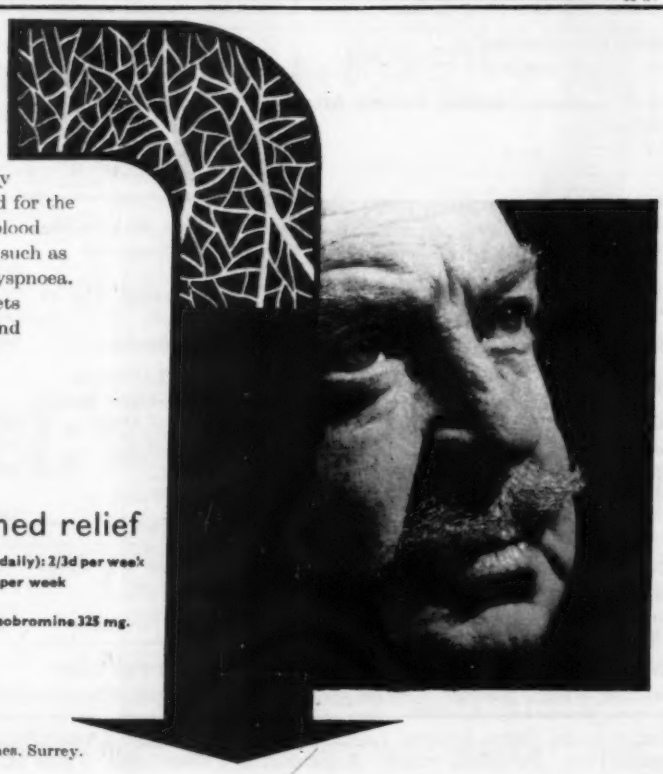

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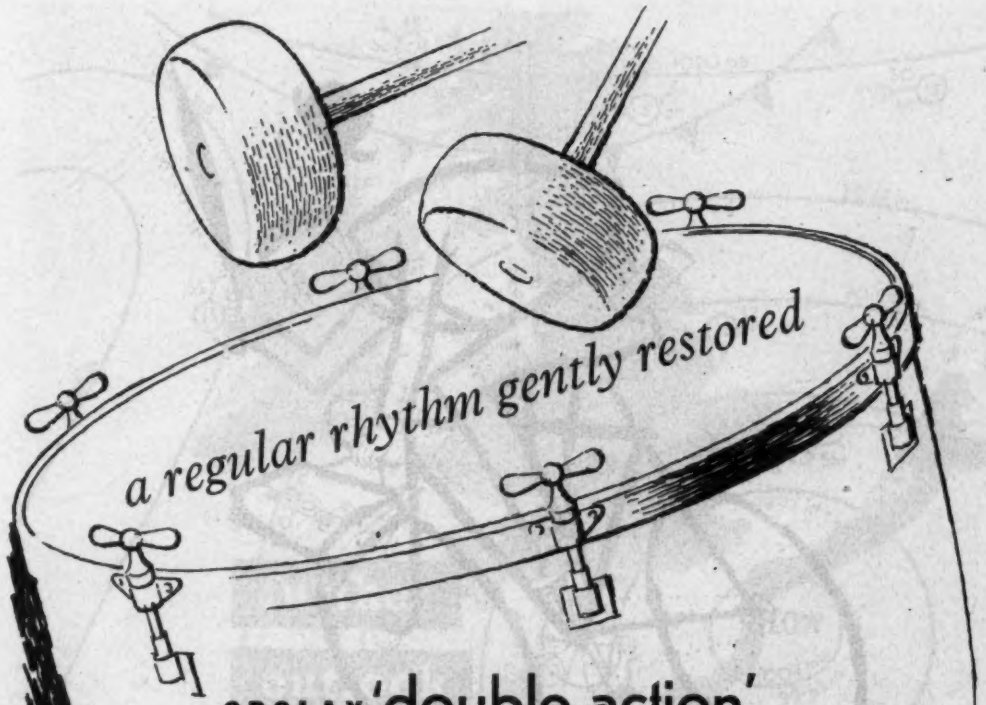

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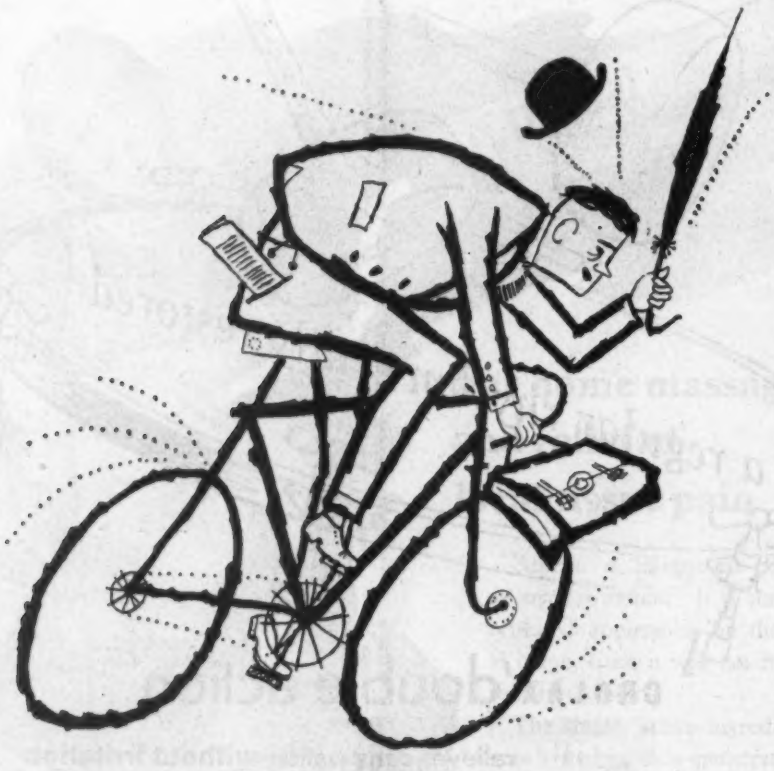

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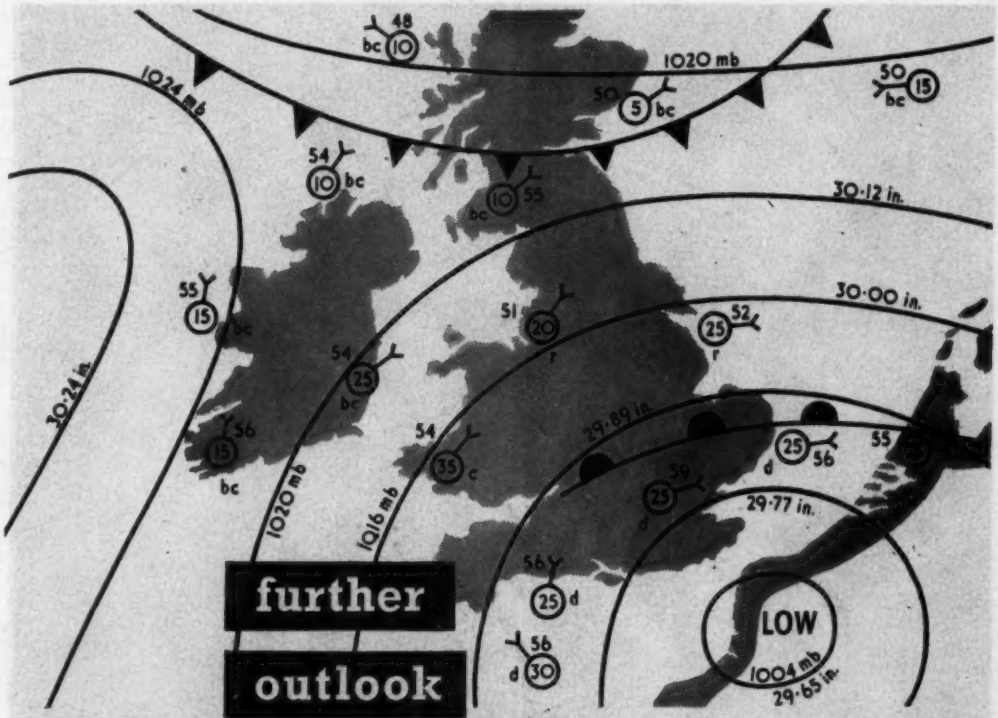

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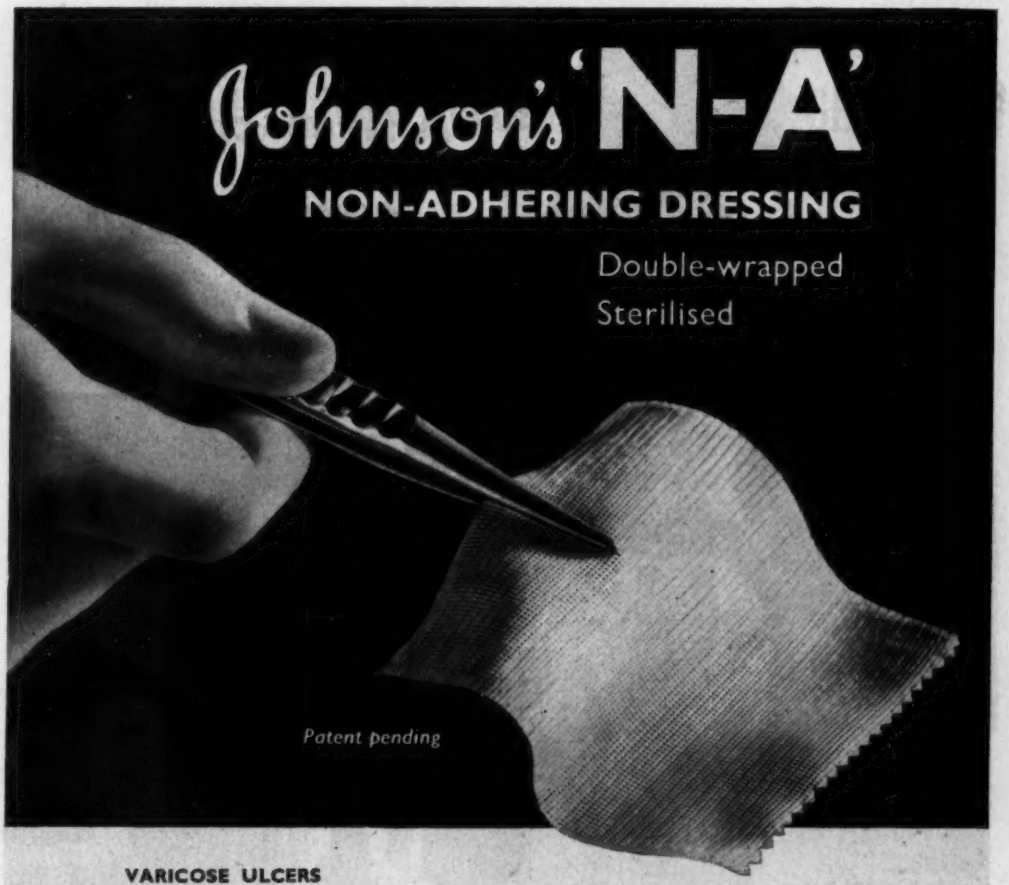

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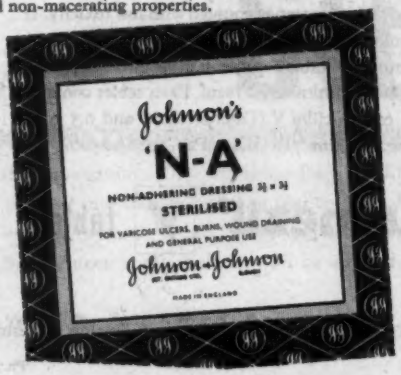

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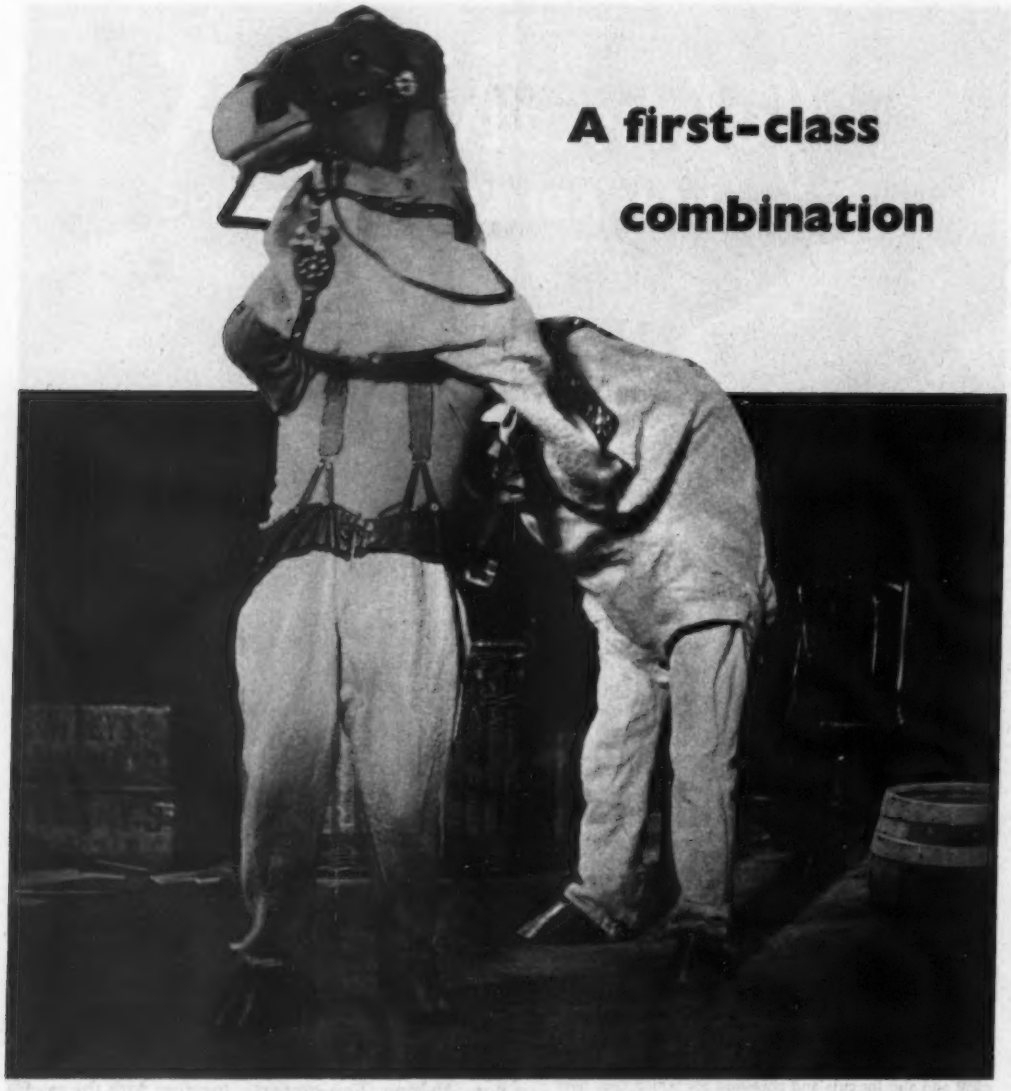

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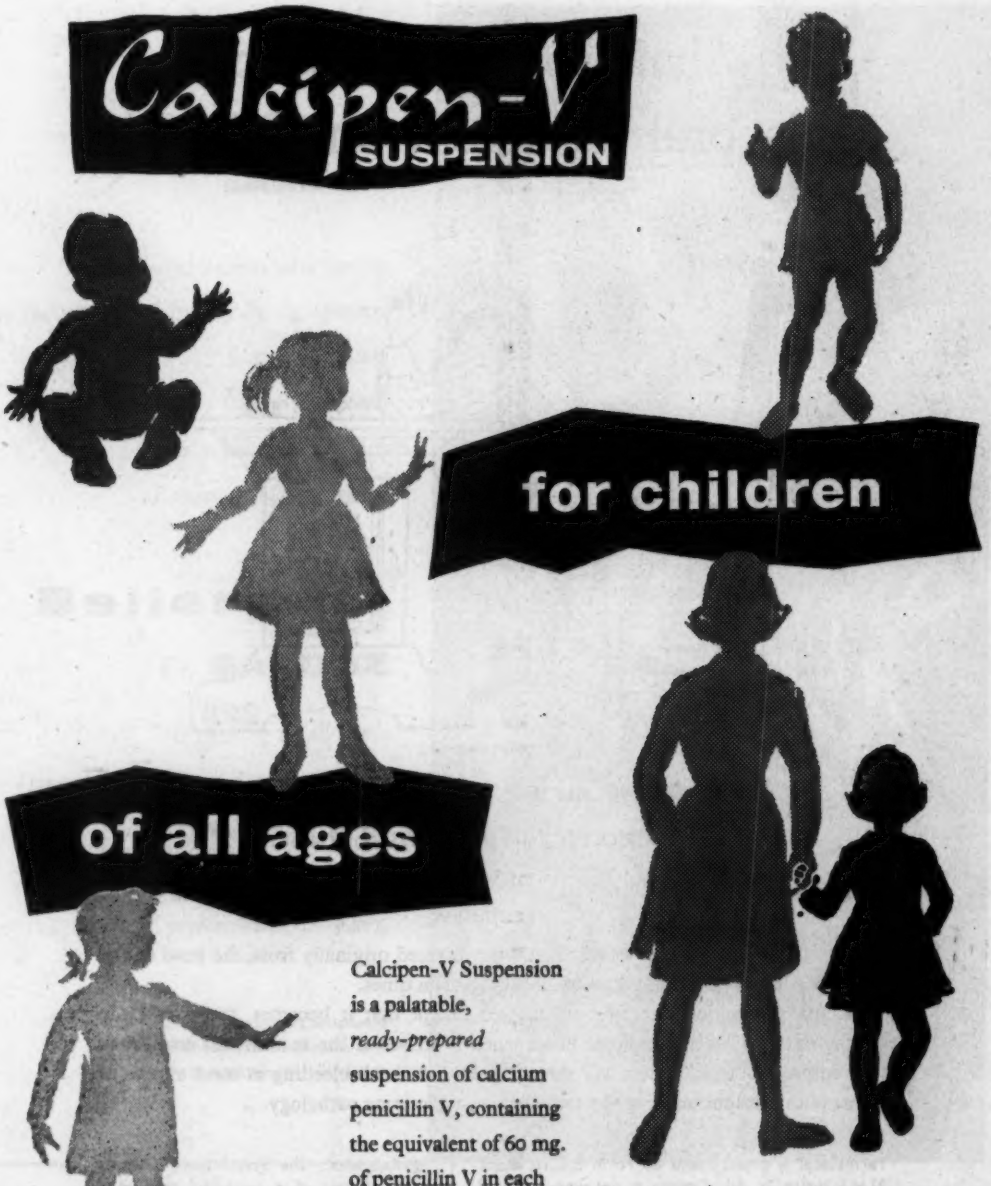

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* *Reference: The Practitioner, February 1957. Report of a successful trial at a London hospital. A summary of this article is available on request.*

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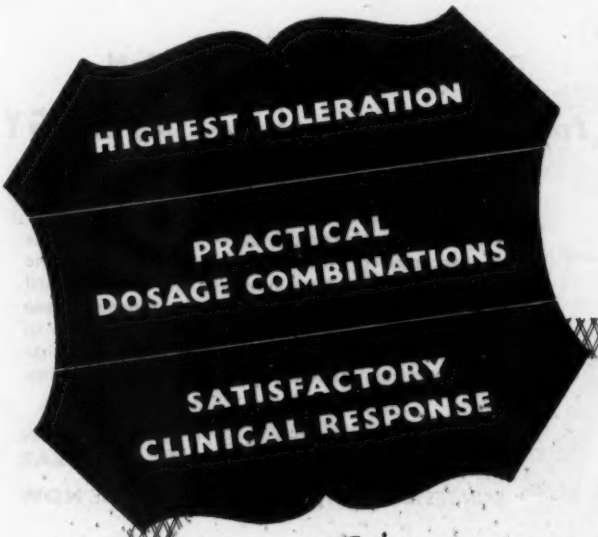

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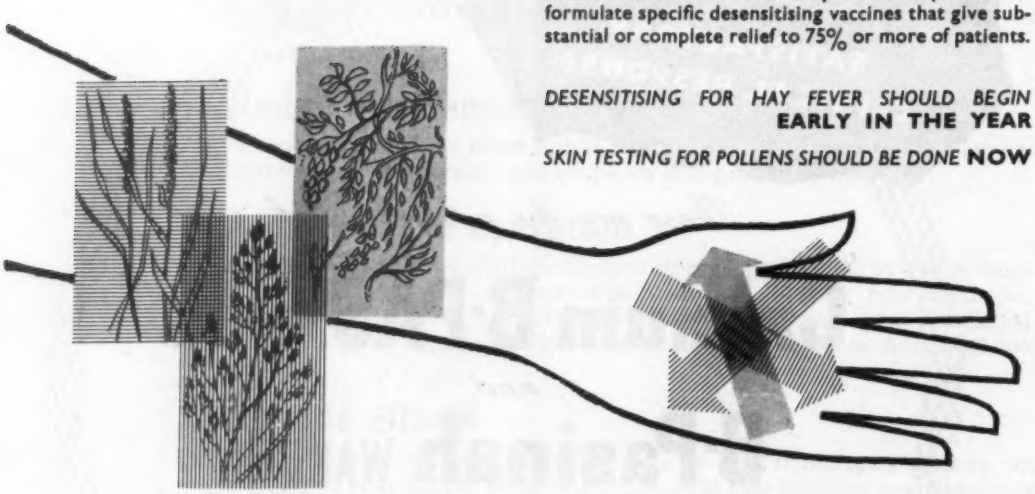

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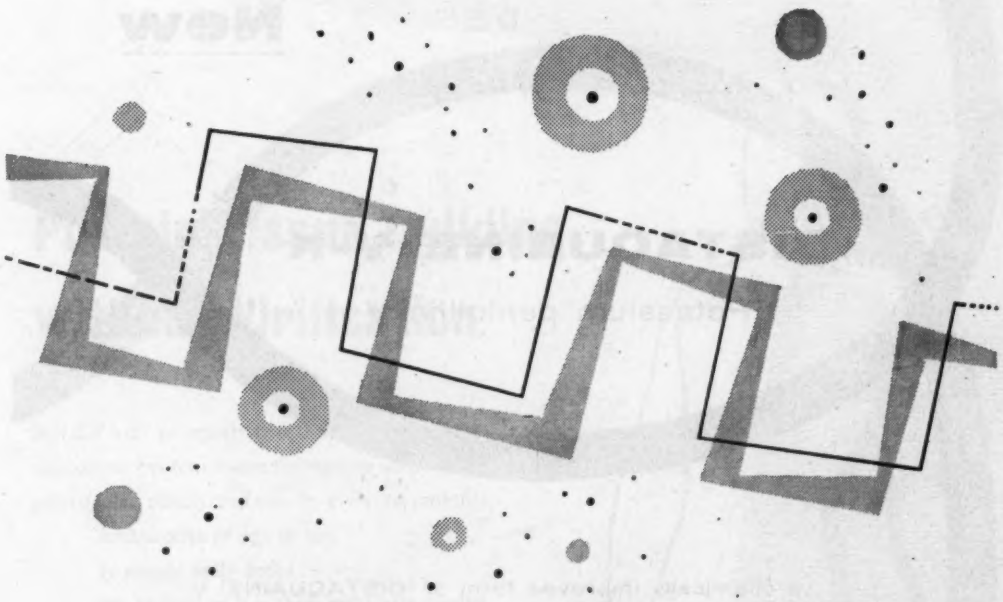

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DISTAQUAINE V-K

Potassium penicillin V

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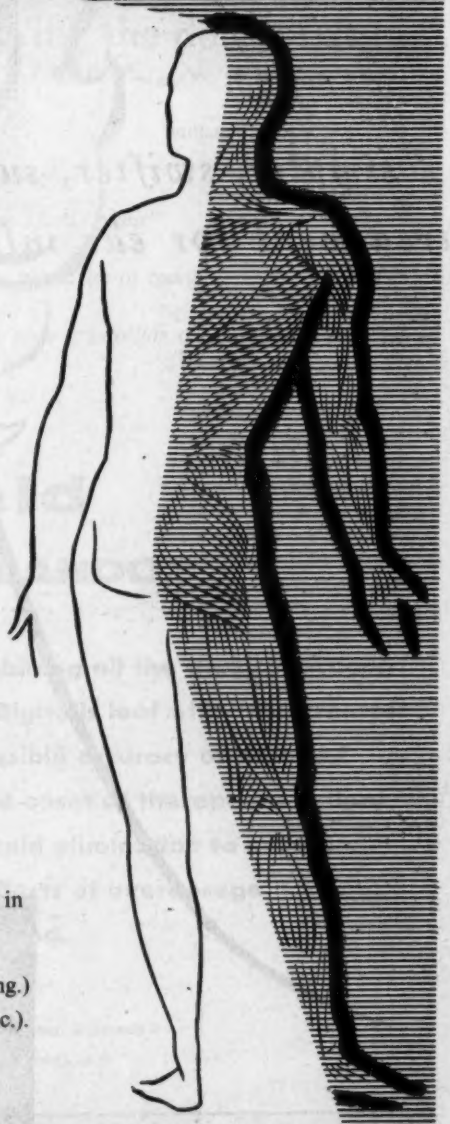

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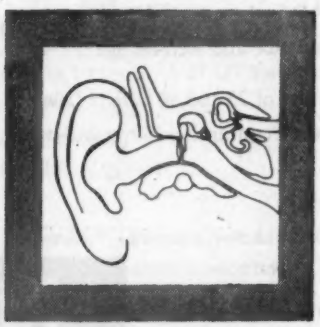

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in the form of the pure crystalline cardiac glycoside

lanatoside C—

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tablets contain 10 mg. P.E.T.N. (pentaerythrityl tetranitrate), a potent coronary vasodilator, and 1 mg. 'Rauwiloid', an alkaloidal fraction of *Rauwolfia serpentina.*

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removes the dread of another attack, and increases exercise tolerance. The need for nitroglycerin is greatly reduced when 'Pentoxylon' is used prophylactically, and in hypertensive patients there is a reduction in blood pressure.

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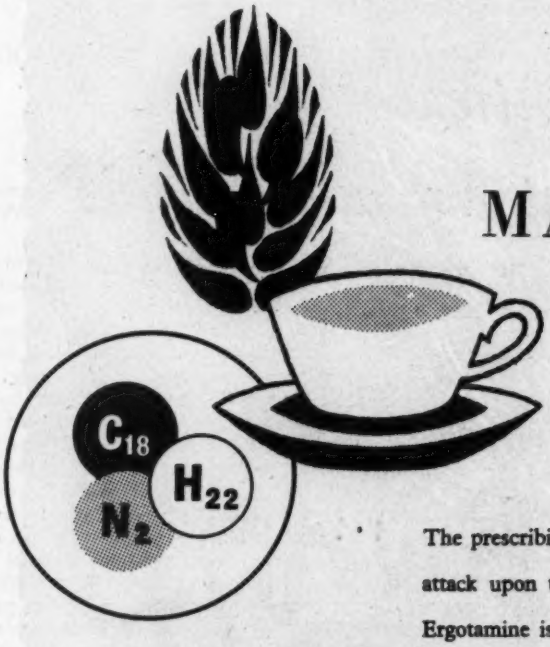

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The prescribing of 'Migril' makes possible at last a *planned* attack upon the three predominant symptoms of migraine. Ergotamine is present at strength in 'Migril' for its specific effect upon the characteristic headache and ocular disturbances. Caffeine is present too, since it acts as a synergist to ergotamine. Frequently, however, ergotamine tends to evoke nausea and vomiting on its own account and can therefore worsen these aspects of the condition. For this reason, the potent, rapidly acting anti-emetic cyclizine is also included in 'Migril'—to overcome any tendency to nausea or vomiting, whether caused by the ergotamine or by the condition itself. And so successfully does cyclizine achieve this aim that truly effective oral doses of ergotamine can today be given—by means of 'Migril'.

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DOSAGE. Adults: Two to six tablets daily immediately after meals.

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PERNIVIT tablets,
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Literature and specimen packings are available on request.

(Medical Department)

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ÆTIOLOGY OF PRE-ECLAMPTIC TOXÆMIA AND ECLAMPSIA

FACT AND THEORY *

F. J. BROWNE

M D. Aberd., D.Sc. Edin., F.R.C.S.E., F.R.C.O.G.

EMERITUS PROFESSOR OF OBSTETRICS AND GYNÆCOLOGY IN THE UNIVERSITY OF LONDON; CONSULTING OBSTETRIC SURGEON, UNIVERSITY COLLEGE HOSPITAL, LONDON

A DISCUSSION at the Royal Society of Medicine, London, on the Ætiology of Pre-eclampsia (*Proceedings of the Royal Society of Medicine* 1957), though of great interest and presenting new data bearing on pathogenesis, seemed to fail in its presentation of all the facts as well as in its lack of any precise conclusions regarding the ætiology of pre-eclamptic toxæmia and eclampsia.

It has long seemed to me that, thanks to the researches in Great Britain, the United States, and elsewhere, especially in the past ten years, we now have all the essential facts bearing on the ætiology of eclampsia, and that they resemble the pieces of a jig-saw puzzle and only need to be assembled in proper sequence to provide an acceptable explanation of eclampsia, including its onset two or three days after delivery.

Any satisfactory explanation of the ætiology of eclampsia must explain (1) why it occurs only in association with pregnancy and only in man; (2) its preference for first pregnancies (75% of cases); (3) why it sometimes occurs in pregnancy with hydatidiform mole and no fœtus, and that very early in pregnancy (say from the 12th to the 16th weeks); (4) why it is five or six times as common in twin as in single pregnancy; (5) why it occurs in 50% of chronic hypertensive pregnancies; (6) its greater frequency in diabetic pregnancy; (7) why it is often associated with "red infarcts" in the placenta, or with concealed accidental hæmorrhage, and sometimes with renal cortical necrosis; and (8) why it often occurs two or three days after delivery (10% of all cases). This last has been the chief obstacle to the acceptance of all published theories, including those of Young (1914), Paramore (1929), Beker (1948), Van Bouwdijk Bastiaanse and Mastboom (1950), Parviainen et al. (1950a and b), Louros and Kairis (1951), Sophian (1953), Theobald (1955), and Bartholomew et al. (1957).

Hormones in Normal Pregnancy

In normal pregnancy the anterior lobe of the pituitary gland hypertrophies and produces excess of corticotrophin. This is no doubt due to œstrogens secreted by the placenta, which, besides the fœtus, is the only new organ in the pregnant woman.

Corticotrophin is also produced by the placenta (Cohen and Kleinberg 1952, Assali, Hamermesz, and Ross 1954). Under this double stimulus the adrenal cortex undergoes hyperplasia and secretes excessive amounts of cortical metabolites, including glucocorticoids (11-oxycorticosteroids), which have an anti-insulin effect on carbohydrate metabolism and are the basis of the well-known delayed sugar-tolerance curve characteristic of normal pregnancy. Under the influence of corticotrophin the adrenal cortex also secretes excess of the mineralocorticoids (11-deoxycorticosteroids), which retain sodium, chloride, and water. Aldosterone, though probably largely responsible for the œdema both of normal pregnancy and of toxæmia, does not seem to be under the influence of the anterior lobe of the pituitary gland or of corticotrophin but to be regulated by sodium and water balance.

At this point let me cite some rather striking evidence of the powerful sodium-retaining and pressor effects of adrenocortical compounds.

Ferrebee et al. (1939) treated 13 cases of Addison's disease with deoxycortone acetate or propionate. This caused a striking retention of salt and water, the urine diminishing to 410 ml. in twenty-four hours in one patient receiving a daily dose of 15 mg. The blood-pressure rose from subnormal to normal levels in two to four weeks, and in 3 of the cases it rose gradually to 160/92, 160/110 and 146/108 mm. Hg. Of the 13 patients 10 developed œdema, varying from mild puffiness of the face and ankles to massive anasarca.

Altschule and Zamcheck (1942) reported the case of a man, aged 43, who had asthma for many years but no evidence of adrenal cortical insufficiency. Because of eczema, which he had had for years, sodium chloride 5 g. by mouth daily and extract of suprarenal cortex 1 ml. daily intramuscularly had been prescribed. At that time his blood-pressure was 120/80 mm. Hg and serum-protein level 5·9 g. per 100 ml. He received altogether 7 ml. of extract of suprarenal cortex in the daily doses. Severe œdema developed in his legs and soon involved his whole body, and in consequence he was admitted to hospital. He then had rapid respiration, dyspnœa, orthopnœa, œdema of face, arms, legs, and trunk, and effusion into his body cavities. His urine contained much albumin, casts, and a few red blood-cells. His blood-pressure was 200/110 mm. Hg and serum-protein level 4·42 g. per 100 ml. There was no evidence of congestive heart-failure. Altschule and Zamcheck considered that "the syndrome closely resembles that produced by a diffusely active vascular toxin". The lowered serum-protein level suggests injury to the capillary walls by the "vascular toxin".

In this connection it is of interest to recall that examination of the œdema fluid in 3 cases of gross œdema in severe pre-eclamptic toxæmia in the obstetric department of University College Hospital, London, showed protein levels of 0·5, 0·57, and 0·9 g. per 100 ml. Since the normal protein level in interstitial fluid is exceedingly low (less than 0·1 g. per 100 ml.), this increase clearly indicates injury to the capillaries, an additional cause of the often rapidly forming œdema of pre-eclamptic toxæmia. Incidentally this demonstration of injury to the capillaries by a vascular toxin justifies the retention of the term "toxæmia of pregnancy".

Though the deoxycortone acetate used by Ferrebee et al. (1939) was a synthetic compound and is probably not produced to any great extent by the adrenal glands, its action in causing œdema and hypertension is of great interest. It is probable that the chief cause of œdema in pre-eclamptic toxæmia is an increased secretion of salt- and water-retaining hormone by the adrenal cortex, but a contributory factor may be antidiuretic hormone, which Hawker (1952, 1957) has shown to be increased in the plasma of patients with pre-eclamptic toxæmia compared with normal pregnancy. Hawker has found too that, in normal pregnancy, this hormone is kept in check by a placental enzyme which does not do so in pre-eclamptic toxæmia.

We shall presently see that hydrocortisone (compound F) can cause in laboratory animals as great a rise of blood-pressure as can deoxycortone acetate. In passing it is

* Paper read at a joint meeting of the Colloquia on Hypertension and Pregnancy Toxæmia and the 4th Conference in Australia of the Royal College of Obstetricians and Gynæcologists, Sydney, Aug. 28, 1957.

important to note that deoxycortone acetate does not raise the blood-pressure in healthy pregnant women. In 1946, during my own investigations of the cause of the hypersensitivity of the vascular system in toxæmia, I was surprised to find that injected extract of suprarenal cortex in the same doses as used by Altschule and Zamcheck (1942) had no effect whatever in raising the blood-pressure in healthy pregnant women. The probable reason for this has now come to light.

Hypertensive effects of Corticotrophin, Cortisone, and Hydrocortisone

Hydrocortisone and cortisone raise the blood-pressure, both systolic and diastolic, in rats at least as much as and probably more than does deoxycortone acetate after two weeks' treatment in intact (non-adrenalectomised) rats (Friedman et al. 1952, Knowlton et al. 1952). It is now well known that hypertension occasionally develops during therapy with corticotrophin and with cortisone (Zweifach and Shorr 1950, Cope and Hurlock 1954). Perera (1950) observed the effect of corticotrophin on the resting blood-pressure of 13 non-pregnant patients; a rise occurred in the great majority. In one patient with hypertension the administration of corticotrophin 100 mg. daily for nine days was followed by a rise of blood-pressure, hypertensive encephalopathy, and mental confusion.

Increase of Corticosteroids in Normal and in Toxæmic Pregnancy

Bayliss et al. (1955) followed the plasma levels of 17-hydroxycorticosteroids at monthly intervals through the normal pregnancies of 30 women. The level rose progressively during normal pregnancy, becoming in some cases very high; after delivery the level fell and was normal again after a week. Gemzell (1953) found that the concentration of 17-hydroxycorticosteroids (which include hydrocortisone) in the blood in the last three months of normal pregnancy was four times the pre-pregnancy value. Immediately after delivery it increased to seven times the normal value, but by the sixth day it had fallen to pre-pregnancy level. The significance of this rise immediately after delivery will be discussed later.

Many investigators have found that, in toxæmia, the urinary excretion of corticosteroids is considerably larger than in normal pregnancy (Tobian 1949, Parviainen 1950a and b, Chart et al. 1951, Lloyd et al. 1952, Venning et al. 1954).

I am aware that Assali et al. (1955) found that the blood levels of 17-hydroxycorticosterones were not raised in toxæmia compared with normal pregnancy. The glucocorticoids alone, however, were estimated, not the mineralocorticoids, which are probably the hormones chiefly involved in pregnancy toxæmia. Assali et al. (1955), commenting on their results, state:

> "By excluding glucocorticoids from involvement in toxæmia our results lend support to the work of the aforementioned investigators (i.e., Venning, Tobian, Lloyd et al.) which indicates that mineralocorticoids may be the hormones involved in this abnormality."

It should be here noted that Chart et al. (1951) found much increased excretion of a sodium-retaining factor in toxæmic pregnancy but no parallel increase in the excretion of 11-oxysteroids (glucocorticoids).

Cushing's Syndrome and Normal Pregnancy

There are several resemblances between normal pregnancy and Cushing's disease, which is now regarded as due, in most cases, to hyperplasia of the adrenal cortex. J. S. L. Browne, indeed, has spoken of normal pregnancy as "a kind of physiological Cushing's syndrome". Examples of this resemblance are insensitivity to insulin, adiposity, osteoporosis, striæ, sodium retention, and hypertension, which is present in Cushing's syndrome in 90% of cases. Study of 15 cases of normal pregnancy by Bush and Pickering (Bush 1953) has shown that the blood-level of 17-hydroxycorticosterone is within the range of that found in Cushing's disease:

> "Thus the increased rate of adrenocortical secretion in pregnancy, indicated by clinical findings and estimations of urinary steroids, is also associated with an increased concentration of adrenocortical hormone in the peripheral venous blood" (Bush 1953).

I have discussed Cushing's syndrome at some length because it shows that blood-pressure-raising hormones are produced by the adrenal cortex in normal pregnancy. I shall suggest later that hypertension similar to that in Cushing's disease would develop in every pregnant woman if it were not for the protective placenta. Striæ often appear in pregnancy on the upper and outer aspects of the thighs, where they could not be due to stretching of the skin or to deposit of fat over the fascia lata. They are very well-known side-effects of cortisone, and though they are usually present in Cushing's disease, even on thin legs, they may be absent, as they often are, in pregnant women.

The Protective Placenta

It will be evident that the normal overaction of the anterior lobe of the pituitary gland and of the adrenal cortex can cause the syndrome of pre-eclamptic toxæmia, including œdema, hypertension, and albuminuria. Why then does not every pregnant woman become hypertensive? That she becomes œdematous is well known, and that half the weight gain of normal pregnancy is due to retention of water—i.e., 12 lb. or 6 litres of water.

In 1948 it was shown that there is present in the normal human placenta and decidua a highly active mono-amine oxidase that can inactivate vasoconstrictor amines—e.g., adrenaline and tyramine. Its activity increases as the placenta matures, and is diminished or inhibited by a decrease in the oxygen tension of the medium in which it acts (Luschinsky and Singher 1948, Thompson and Tickner 1949). The significance of this work could not be appreciated in 1948, because no work had been done on the maternal placental blood-flow. Browne and Veale (1953), however, by injecting radioactive sodium into the placental blood sinuses and measuring its rate of disappearance in healthy, pre-eclamptic, and chronically hypertensive women, showed that there was a reduction of about half in the pre-eclamptic and chronically hypertensive women compared with the healthy women. This reduction could decrease the oxygen tension within the placenta, and the finding of a decreased oxygen tension in the cord blood in toxæmia (Walker 1954) suggests that this actually happens.

It will be clear, therefore, that in normal pregnancy, when the placenta has not been made ischæmic, pressor substances can be wholly or partly destroyed; in placental ischæmia, however caused, the enzyme cannot exert its anti-pressor activity, with consequent failure of degradation of vasoconstrictor substances produced by the adrenal glands.

Corroborative evidence of this activity is found in the fact that, though corticotrophin causes hypertension in non-pregnant women, it does not do so in healthy pregnant women. Assali and Suyemoto (1954) gave intramuscular corticotrophin 120 mg. for four, five, and

six days to 3 normotensive pregnant women. There was retention of sodium, but the blood-pressure was not raised nor the weight increased. These data, they say,

"show that ACTH does not cause changes in the electrolytes in the pregnant woman of the same magnitude as in the non-pregnant state. Although some decrease in sodium excretion and some increase in potassium excretion occurred these changes were not as significant as those observed by Forsham et al. (1948) in non-pregnant women, even though the dose used was three times as great. Also the decrease in eosinophile counts and increase in uric acid and 17-ketosteroids never reached the marked levels obtained in non-pregnant subjects . . . The lack of striking response is probably due to a certain tolerance of the pregnant woman to ACTH."

Neither can deoxycortone acetate, which we have seen is such a potent hypertensive and sodium-retaining agent in non-pregnant women, cause hypertension in pregnancy.

Assali et al. (1953) gave intramuscular deoxycortone acetate 30 mg. daily for four days in the last three months of normal pregnancy, together with 9 g. of salt and a normal hospital diet, and failed to induce any of the changes seen in toxæmia.

Margulis et al. (1954) write: "One of the most striking observations" (in their research on the use of corticotrophin and cortisone in pregnancy) "was the increased tolerance of pregnant patients to the administration of ACTH and cortisone.

After discussing several possible reasons for this they speculate on "the production of a physiological antagonist".

Ferguson (1951) had previously noted that "the pregnant woman appears peculiarly resistant to ACTH as she fails to show the expected physiological changes". He also failed to get retention of water after corticotrophin therapy. This led him to conclude that "adrenocortical stimulation is probably not the cause of positive water balance in pre-eclamptic toxæmia".

I have already mentioned my own failure to cause hypertension by injection of extract of suprarenal cortex into healthy pregnant women.

Causes of Placental Ischæmia

We have seen that pre-eclamptic toxæmia and eclampsia are more common in first and twin pregnancies. Overdistension of the uterus in twin pregnancy and its stretching against powerful resistance in primigravidæ seem to be a sufficient explanation. In twin pregnancy the blood-supply to the wall of the uterus is significantly reduced (Morris et al. 1955); it is a reasonable assumption that this is due to overdistension. It will be appreciated that, since pre-eclamptic toxæmia occurs in only 10% of primigravidæ and 5% of multiparæ, a diminished blood-flow through the uterine wall would, on average, be found in only 1 of every 10 primigravidæ and 1 of every 20 multiparæ.

An alternative suggestion is that of Beker (1948), approved and adopted by Van Bouwdijk Bastiaanse and Mastboom (1950), that the uterus in young primigravidæ often has a hypoplastic vascular system, which is permanently improved after one or two pregnancies. The figures illustrating Beker's paper are certainly very impressive.

In *chronic hypertension* peripheral vasoconstriction (expressed as raised diastolic pressure) reduces the placental blood-flow; hence the increased liability of chronic hypertensives to develop pre-eclamptic toxæmia.

Association of Eclampsia and Pre-eclamptic Toxæmia with Placental Red Infarcts, Uteroplacental Apoplexy, and Renal Cortical Necrosis

All these are explained by arterial spasm. Clinical experience shows that, when the systolic blood-pressure rises above 160 mm. Hg, especially if it rises quickly, these accidents are liable to happen. The spasm in the spiral arteries of the decidua—an exceedingly vascular area—temporarily cuts off the blood-flow through the arterioles and capillaries distal to the constriction and so injures their walls by anoxia. After some time the constriction relaxes, blood flows again through the vessels, and their injured walls give way, with the result that hæmorrhage takes place in the decidua underneath the placenta. It may be small, causing the well-known "red infarct" described by Young (1914); in this case the fœtus usually survives for the time being. The hæmorrhage may be large enough to separate a large part of the placenta, almost always followed by death of the fœtus. It will be obvious that this is the same mechanism that causes normal menstruation as described by Markee (1940), though the cause of the vasoconstriction is, of course, different. Similar vasoconstriction in the kidney can injure glomeruli and cortex, with results varying in severity and extent according to the duration of the spasm, from albuminuria in the mildest to irreversible bilateral cortical necrosis in the most extensive and prolonged (Sheehan and Moore 1952).

Toxæmia in Diabetic Pregnancy

The most generally accepted theory of the ætiology of diabetes mellitus is that excess of growth hormone from the anterior lobe of the pituitary gland stimulates the β cells of the islets to produce abnormally large amounts of insulin, and that this overproduction exhausts the β cells, which then degenerate and die. If this is the cause, it is strange that not every diabetic develops hypertension and œdema, because one would expect that the overacting anterior lobe of the pituitary gland would at the same time secrete excess of other hormones, including corticotrophin. There is, however, no evidence that it produces excess of gonadotrophic hormone, and it seems probable that growth hormone alone is in excess. One cannot therefore explain the increased incidence of toxæmia in diabetic women by increase of corticotrophin acting on the adrenal glands. Another possibility is that atheroma of the pelvic arteries, which is present in most diabetics after they have had the disease for twenty years or more, limits the blood-supply to the placenta. White (1952) states that it is in the severe grades of diabetes, in which there is arterial disease, that toxæmia is likely to arise.

Toxæmia in Hydatidiform Mole

The chorionic villi normally secrete corticotrophin, but whether it is the cytotrophoblast or the syncytium that does so is unknown. It is of course well known that the cytotrophoblast secretes excessive amounts of chorionic gonadotrophin in hydatidiform mole, and it may reasonably be assumed that corticotrophin is also in excess. If so, it would explain the liability to toxæmia and even eclampsia in molar pregnancy, even in the first three months. It is also probable that the dropsical chorionic villi so fill the intervillous spaces that maternal blood is squeezed out and oxygen tension reduced.

Eclampsia after Delivery

After the birth of the placenta its protective action, poor though it may have been because of placental ischæmia in toxæmia, is suddenly withdrawn. Pressor substances are still being produced by the adrenal cortex, but in rapidly diminishing amounts, and are now free to circulate in the maternal blood. We have already seen that Gemzell found an increase of almost 100% in the blood-level of 17-hydroxycorticosteroids immediately after delivery. I suggest that this is the explanation of

eclampsia within the first three days of the puerperium. Fits occurring after that time are, I suggest, due to one of two causes: primary cerebral venous thrombosis (Martin and Sheehan 1941) and subarachnoid hæmorrhage. In all such cases a neurologist should be called in and, when subarachnoid hæmorrhage is a possibility, lumbar puncture should be done to exclude blood in the cerebrospinal fluid.

If this explanation of the absence of hypertension in normal pregnancy and of the occurrence of eclampsia in the first three days after delivery is correct, we would expect a rise of blood-pressure after the birth of the placenta in women whose blood-pressure has been normal throughout pregnancy and labour. I have not been able to find any reference to this in textbooks, and it seems to have been assumed that the blood-pressure is always normal. Examination of blood-pressures of such women at the Royal Hospital for Women, Sydney, and at the Postgraduate Medical School of London, has, however, shown that 20–30% are hypertensive in the first three days after delivery. This is remarkable when it is considered that these women are at rest, are tired after labour, and have often lost a considerable amount of blood. Intramuscular ergometrine 0·5 mg. was given routinely at the end of the second stage, but the puerperal blood-pressures were not taken until between twelve and twenty hours after delivery, and some much later. It is therefore unlikely that any of the hypertensions were due to ergometrine.

Rise of Blood-pressure in Toxæmic Patients after Delivery

During the last week several examples of this have come to my notice without seeking or searching.

(1) Mrs. A, aged 27, first pregnancy, multiple pregnancy, and pre-eclamptic toxæmia. *May 1, 1957:* membranes stripped and medical induction given. *May 3:* artificial rupture of membranes and oxytocin drip. *May 4:* episiotomy and breech extraction of first infant, forceps delivery of second; manual removal of placenta because of postpartum hæmorrhage; intramuscular ergometrine 0·5 mg. given; after delivery blood-pressure rose remarkably to 170/120 mm. Hg. From this time onward the patient progressively deteriorated and died at 1.45 A.M. on *May 5*. Necropsy revealed a liver with findings typical of eclampsia.

(2) Bulfin and Lawler (1957) review 234 sets of twins delivered beyond seven months' gestation, and state that there were 12 cases "in which the excessive rise in blood pressure post-partum resulted in headache, nausea and visual disturbances, creating all the appearances of impending eclampsia. In retrospect we now feel that the injudicious use of ergonovine in these patients already toxæmic could have been responsible for the fulminating post-partum symptoms." They state that intravenous ergometrine maleate occasionally causes acute hypertension which persists from half an hour to four hours. "The hypertensive effect of this drug seems to be even more pronounced in the patient whose uterus is contracting following distension from a twin pregnancy."

(3) Dugan and Black (1957), discussing kyphoscoliosis in pregnancy, review 39 pregnancies in twenty-two hospitals and give a detailed account of 1 fatal case. This woman had toxæmia and was delivered vaginally by forceps after pudendal block. The placenta and membranes were complete, and there was no postpartum bleeding. At 2.30 P.M., forty-five minutes after delivery, the patient's pulse-rate was 122 and blood-pressure 148/80 mm. Hg. At 3.30 P.M., one and three-quarter hours after delivery, her blood-pressure was 180/100 mm. Hg. She had a generalised convulsion, which lasted about three minutes. Her condition steadily deteriorated, and she died at 7 P.M. During labour she had been given pethidine and scopolamine and, because of severe restlessness during delivery, intravenous morphine sulphate gr. $^1/_6$. There is no note about whether ergot was given or not.

Eclamptic Fits

These are caused by a rapidly rising systolic blood-pressure causing hypertensive encephalopathy, and by cerebral œdema.

That a rapidly rising systolic blood-pressure alone can cause convulsions is shown by Byrom's (1954) experiments on rats. He removed one kidney and clamped the renal artery of the other. In the weeks after the operation the systolic blood-pressure rose and ultimately, when it reached an excessively high level (over 200 mm. Hg), especially if it rose steeply, fatal convulsions came on. Through a 'Perspex' window in the rat's skull spasm was seen in the cerebral arterioles during the convulsions.

Œdema of the brain alone can cause fits. Rowntree (1923) showed that by giving 50 ml. of water per kg. of body-weight to dogs every half-hour—i.e., faster than the kidneys could excrete it—he could produce convulsions, coma, and death in a few hours. Necropsy revealed œdema of the connective tissues, liver, kidneys, and brain. Rowntree demonstrated increased intracranial pressure during life and believed this to be the cause of the convulsions.

It is possible that hypertension and œdema can supplement each other as eclamptogenic agents; that fits can occur if systolic blood-pressure rises quickly to a high level with little or no œdema, as in Byrom's (1954) rats; and that they may occur if there is cerebral œdema alone if the blood-pressure is normal or near normal, as in Rowntree's (1923) dogs.

Cerebral dysrhythmia may possibly predispose to fits, but the evidence is inconclusive (Rosenbaum and Maltby 1943, Parviainen et al. 1950a and b, Macintosh 1952, James 1955, Poidevin 1955). Recently I saw a patient who had pre-eclamptic toxæmia and idiopathic epilepsy, but eclampsia did not develop.

This view of the cause of eclamptic fits received support from the results in Cincinnati, U.S.A., where treatment of eclampsia is based on the assumption that the fits are due to cerebral vascular spasm, and that if it is relieved they will cease. This is achieved by giving alkaloids of veratrum viride; œdema is also treated with intravenous dextrose; and magnesium sulphate, 50% solution, is injected intramuscularly as a sedative and anticonvulsant to relax the cerebral vasospasm (McCall and Sass 1956). No other sedatives are given. To date 205 consecutive cases have been reported with only 3 deaths, 2 of which took place in pre-antibiotic days from puerperal sepsis, one fourteen days and the other sixty-five days after cure of the eclampsia and delivery. This is an uncorrected maternal mortality of 1·5% (Bryant and Fleming 1940, Garber 1953).

Role of Diet in Causing Toxæmia

The greatly increased frequency of eclampsia in patients with beriberi (King and Ride 1945) and in areas of the United States where pellagra is endemic suggests that vitamin-B complex may be essential for the action of the placental enzymes. Hipsley (1953) has found that eclampsia is much less common among races that consume large amounts of fibre in their diet. I think that the fibre may contain vitamin B. Possibly other dietary factors—e.g., calcium and vitamin D—are also important in this connection (Theobald 1955). Perhaps a high-carbohydrate diet, by raising the blood-sugar level, calls for a greater output of insulin and therefore of growth hormone to provide it, and as a consequence of this an increased output of corticotrophin. This might explain the value of a low-carbohydrate diet in preventing toxæmia (Stevenson 1952, Hamlin 1952, J. Woodhill, personal communication, and others).

Sensitisation of Vascular System

That the vascular system is hypersensitive in pre-eclamptic toxæmia was first demonstrated by Schockhaert and Lambillon (1937) and Dieckmann and Michel (1937), and confirmed by De Valera and Kellar (1938) and myself (Browne 1943).

That this hypersensitivity is not hereditary or constitutional but acquired between about the seventeenth week and the time at which toxæmia becomes clinically manifest was shown by me in 1946 (Browne 1946), when I found evidence that its cause was chorionic gonadotrophin. This finding that the sensitisation is acquired in the course of pregnancy rules out the suggestion that pre-eclamptic toxæmia develops only in women with a familial predisposition to chronic hypertension. I was unable to pick out, by the cold pressor test, women who would develop toxæmia in later pregnancy (Browne 1940).

Byrom (1937) produced, in rats, lesions closely resembling those of eclampsia—focal necrosis of the liver and symmetrical cortical necrosis in the kidneys—by injecting vasopressin. He believed the lesion to be due to arteriolar spasm. He also found that the sensitivity to vasopressin could be increased ten times by œstrogenic hormones, and that, in unspayed rats, the sensitisation could equally well be brought about by gonadotrophic hormones.

All the evidence therefore goes to show that sensitisation of the vascular system, acquired from whatever cause in pregnancy, plays a part in the ætiology of toxæmia.

I am aware that the adrenocorticosteroids are not mono-amines. They are all combinations of carbon, hydrogen, and oxygen, and I suggest that the normal placenta contains an oxygen-sensitive oxidase that can inactivate them. This is a matter for further investigation.

What is the purpose of this elaborate mechanism that has been developed during the course of normal pregnancy in the internal secretory organs, including the placenta? I suggest that it is designed to protect the fœtus from the dangerous consequences of low blood-pressure that would otherwise occur, and increase as pregnancy advances, through pooling of blood in the maternal placental blood lake combined with the erect posture (Theobald 1955). The result is that, in the great majority of cases, the blood-pressure is nicely adjusted to that end and kept at normal levels, neither hypotensive nor hypertensive, by the protective placenta. Through various causes this healthy adjustment sometimes fails, and pre-eclamptic toxæmia and eclampsia are the consequences. There is no need to think of them as "diseases of adaptation", because the stimulus for the adrenal cortex is in the placenta.

Summary

Under the influence of corticotrophin produced by the placenta and the anterior lobe of the pituitary gland (the latter stimulated by œstrogens secreted by the placenta) the adrenal cortex in pregnancy produces excess of cortical metabolites, including glucocorticoids and mineralocorticoids.

There are several resemblances between normal pregnancy and Cushing's syndrome, which is usually due to hyperplasia of the adrenal cortex and is in 90% of cases accompanied by hypertension. In normal pregnancy there must therefore be a pressor substance produced in excess (compared with the non-pregnant individual) by the adrenal cortex. The blood in normal pregnancy contains 17-hydroxycorticosteroids equal in amount to or exceeding those in Cushing's syndrome.

Every pregnant woman would become hypertensive if it were not for the protective placenta which furnishes, it is suggested, an oxygen-sensitive oxidase that inactivates pressor hormones from the adrenal cortex. The presence of this enzyme would explain the fact that cortical hormones, which in the non-pregnant individual cause hypertension and œdema, are without effect in healthy pregnant women. If from any cause the placenta is made ischæmic and its oxygen tension lowered, the protective enzyme is made ineffective, and hypertension results.

The excess of chorionic gonadotrophin present in pre-eclamptic toxæmia can be explained by its non-destruction. There is evidence that it causes the hypersensitivity of the vascular system known to exist in pre-eclamptic toxæmia.

In 25–30% of women who have been normotensive during pregnancy and labour the blood-pressure reaches hypertensive levels in the first three days after delivery. This can be correlated with Gemzell's (1953) findings that the level of 17-hydroxycorticosteroids in the blood before labour is increased by nearly 100% immediately after the birth of the placenta. Dangerous eclamptogenic rises of blood-pressure often occur in toxæmic patients after delivery. It is suggested that the birth of the placenta and the loss of its inactivating effect on pressor hormones explain the onset of eclampsia in the first three days of the puerperium in women who have had pre-eclamptic toxæmia before delivery.

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CHLOROTHIAZIDE: AN ORAL DIURETIC

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MERSALYL and other mercurial compounds given by injection usually produce a satisfactory diuresis in œdematous patients, and act by increasing the renal excretion of chloride, which is accompanied by increased urinary loss of sodium and water. But the search for an orally effective diuretic has continued because parenteral administration is unpleasant and even painful for the patient, and inconvenient for the doctor or the nurse. In recent years several such substances have been introduced, but unfortunately none has so far proved as potent as mersalyl.

Mercurial compounds when given by mouth have less diuretic action, and if their dosage is increased they readily induce intestinal colic and diarrhœa.

Acetazolamide ('Diamox'), a carbonic anhydrase inhibitor, produces a diuresis by increasing the urinary loss of bicarbonate, which is accompanied by increased excretion of sodium, potassium, and water. After a few days' continued administration acetazolamide loses its efficacy, and its action is self-limiting because a metabolic acidosis develops and the amount of bicarbonate filtered by the glomeruli is reduced (Counihan et al. 1955). Thus Hanley and Platts (1956) found it less effective than mersalyl, and Relman et al. (1954) concluded that, in patients with severe congestive cardiac failure, it was of little or no clinical value.

Aminometradine ('Mictine'), another non-mercurial diuretic, may take several days to produce its maximum effect (Hanley 1956), and has to be discontinued in a third of patients because of anorexia, nausea, and vomiting (Wener and Knight 1957).

We relate here our initial experience with a new non-mercurial diuretic, chlorothiazide. This substance was first synthesised by Novello and Sprague (1957), and the free SO_2NH_2 group in its molecule (fig. 1) suggested that it would be a carbonic anhydrase inhibitor. Although it has this effect in vitro (Beyer et al. 1957), its diuretic action in man is largely due to enhanced excretion of chloride ions with an almost equimolar loss of sodium, and, compared with acetazolamide, increased excretion of bicarbonate is neither marked nor constant (Ford and Spurr 1957, Beyer 1958, Bayliss et al. 1958). Thus by increasing chloride excretion the action of chlorothiazide is similar to that of mercurial diuretics.

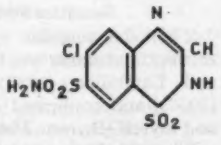

Fig. 1—Chlorothiazide (6-chloro-7-sulphamyl-1,2,4, benzothiadiazine-1, 1-dioxide).

Patients and Methods

The response to chlorothiazide was studied in twenty-four patients, of whom seventeen had congestive cardiac failure and the remainder various other causes of œdema (table I).

All were inpatients, except three with premenstrual œdema and a cirrhotic patient with œdematous legs following a porta-caval anastomosis. Thirteen had been treated in hospital for periods ranging from 6 to 180 days before chlorothiazide was given, and many of these were severely ill, having shown little or no improvement on standard methods of treatment, including injections of mersalyl. In others the period of observation before chlorothiazide therapy was brief because of the severity of their symptoms.

As far as possible a steady state was obtained before chlorothiazide therapy was started, and if other treatment was being given this was kept constant throughout. The daily intake of sodium was unrestricted in the patients with premenstrual œdema but limited to 22, 43, 87, or 218 mEq. in the others (table I). The intake of fluid was unrestricted. The patients were weighed daily, and the urine of inpatients was collected in 24-hour periods. Serum-electrolytes were measured weekly.

In eleven patients the daily urinary excretion of sodium, chloride, and potassium was determined, and in a few the extracellular fluid volume was measured before and after treatment. Hæmoglobin estimations, white-cell and platelet counts and liver-function tests were done weekly in the first five patients treated.

Sodium and potassium were measured by flame photometry; chloride by mercuric-nitrate titration (Schales and Schales 1941); carbon dioxide by the method of Peters and Van Slyke (1932); and extracellular fluid with radiobromine (Nicholson and Zilva 1957).

The usual dose of chlorothiazide, supplied in 500 mg. tablets, was 2 g. daily, 1 g. being given at 8.30 A.M. and 1 g. at 4.30 P.M.

Results

The response to chlorothiazide, assessed according to the fall in bodyweight, the reduction in œdema, and the development of biochemical abnormalities, was defined as follows:

Good, when the œdema disappeared and no biochemical abnormality developed.

Fair, when the œdema (1) failed to clear completely, (2) disappeared initially but returned if the patient became more active or was given a diet containing more sodium chloride, or (3) disappeared only when mersalyl was given in addition to chlorothiazide; or when biochemical abnormalities developed.

Poor, when there was no significant loss of weight or reduction in œdema, or, as happened in one patient, chlorothiazide was discontinued because of malaise.

Tables I and II summarise the results. In patients who responded, chlorothiazide caused an approximately equimolar loss of chloride and sodium (as shown by the sodium and chloride excretion in fig. 2 from day 48 onwards, and in fig. 3 from day 24 onwards). Usually the increase in water and sodium excretion was as great on the first day as on any subsequent day (fig. 2), but in two

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TABLE I—PATIENTS TREATED WITH CHLOROTHIAZIDE

Case no.	Age (yr.)	Diagnosis	Previous response to mersalyl	Days in hospital before chlorothiazide therapy	Intake of sodium (mEq./daily)	Loss of weight on chlorothiazide therapy (lb.)	Response to chlorothiazide	Remarks
1	72	I.H.D.	Poor	47	87	15	Good	Fig. 2
2	52	I.H.D.	Not tested	4	218	8	Good	..
3	68	I.H.D.	Not tested	1	87	11	Good	..
4	78	I.H.D.	Not tested	1	87	14	Good	..
5	55	I.H.D.	Poor	20	87	7	Fair	Increased activity required chlorothiazide and mersalyl for control of œdema
6	78	I.H.D.	Poor	180	22	0	Poor	No response. Died
7	71	H.H.D.	Poor	6	22	27	Good	Fig. 3
8	61	H.H.D.	Poor	77	22	44	Good	..
9	60	H.H.D.	Poor	21	87	10	Good	..
10	59	H.H.D.	Not tested	28	218	14	Good	..
11	64	H.H.D.	Not tested	3	87	9	Good	..
12	57	H.H.D.	Poor	9	87	11	Fair	Œdema returned on increased intake of salt; complicated by hypoproteinæmia; hypokalæmia
13	67	H.H.D.	Poor	10	43	6	Fair	Renal insufficiency; blood-urea level rose from 50 to 150 mg. per 100 ml.
14	72	H.H.D.	Not tested	5	87	8	Fair	Œdema returned on increased activity
15	83	A.I.	Not tested	7	218	10	Good	..
16	55	A.I.	Poor	54	22	15	Fair	5 lb. loss on chlorothiazide therapy; further 10 lb. loss when mersalyl added
17	21	A.I., M.S. & T.I.	Poor	38	22	0	Poor	No significant response; depletion of potassium. Died
18	30	Pre-menstrual	Not tested	..	N	..	Good	Fig. 4
19	37	Pre-menstrual	Not tested	..	N	..	Good	..
20	43	Pre-menstrual	Not tested	..	N	..	Good	..
21	46	Cirrhosis	Not tested	4	87	7	Poor	Malaise and anorexia
22	38	Nephrosis	Not tested	33	218	26	Fair	Complicated by hypoproteinæmia. Hypokalæmia
23	64	Malignant obstruction of I.V.C.	Poor	6	87	13	Good	..
24	49	Cirrhosis; portacaval anastomosis	Not tested	..	87	5	Fair	Intermittent treatment. Hypokalæmia

A.I., aortic incompetence. I.H.D., ischæmic heart-disease. M.S., mitral stenosis. T.I., tricuspid incompetence.
H.H.D., hypertensive heart-disease. I.V.C., inferior vena cava. N, normal unrestricted sodium intake.

patients the maximum response was not obtained until the 3rd or 4th day. As the œdema subsided and the weight loss levelled off, the sodium and water diuresis diminished.

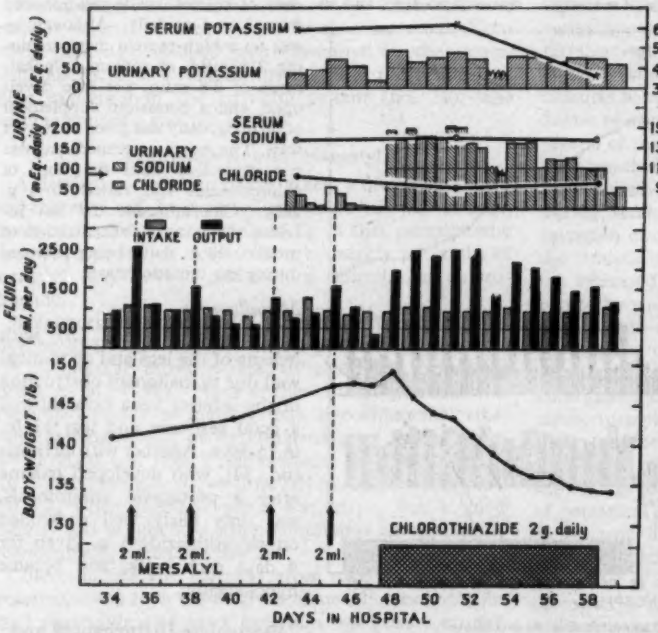

Fig. 2—Patient no. 1, aged 72, with ischæmic heart-disease.

The dietary sodium intake (87 mEq. daily) is indicated by the arrow on the sodium and chloride scale. Note poor response to injections of mersalyl on days 38, 42, and 45 with progressive increase in weight, and satisfactory diuresis when 2 g. chlorothiazide daily is started on day 48. There is also some increase in urinary-potassium excretion and fall in the serum-potassium level. (On day 53 urinary collection was incomplete.)

Congestive Cardiac Failure

Ischæmic heart-disease.—Four of the six patients showed a good response. For example, patient no. 1, who had been in hospital for 47 days, was becoming increasingly œdematous despite bi-weekly injections of mersalyl. On chlorothiazide he lost 15 lb. in 11 days and became œdema-free (fig. 2). Patient no. 5 lost only 3 lb. in 3 weeks when receiving mersalyl bi-weekly, but the addition of chlorothiazide caused an immediate diuresis, the weight falling another 7 lb. in the next 7 days. Although the patient was œdema-free at this time, increased activity caused some re-accumulation of fluid, which required both chlorothiazide and mersalyl for its control; this response was therefore classified as fair. Patient no. 6, who had been in hospital for 6 months with irreversible congestive failure, did not respond to chlorothiazide or mersalyl, singly or in combination, and died.

Hypertensive heart-disease.—Of the eight patients in this group, five showed a good response to chlorothiazide, and three of these (nos. 7–9) were refractory to mersalyl despite normal serum-electrolyte levels. One (no. 7) lost 27 lb. in weight (fig. 3), and another (no. 8), who had been in hospital 77 days and was mersalyl-resistant, lost 44 lb. when chlorothiazide was given.

In three patients the response was only fair:

A grossly obese hypertensive patient (no. 12) with hypoproteinæmia responded initially

TABLE II—SUMMARY OF RESULTS

Disease	Response*		
	Good	Fair	Poor
Congestive heart-failure:			
Ischæmic heart-disease	4	1	1
Hypertensive heart-disease	5	3	0
Valvular heart-disease	1	1	1
Hepatic cirrhosis	0	0	1
Nephrosis	0	1	0
Premenstrual œdema	3	0	0
Miscellaneous	1	1	0
Total	14	7	3

*See text.

with a weight loss of 15 lb. in 9 days. The serum-potassium level fell; and, when the sodium intake was increased from 87 to 218 mEq. per day, the œdema recurred with a weight gain of 4 lb.

Another hypertensive patient (no. 13), with renal insufficiency, lost 12 lb. spontaneously during the first 10 days in hospital. When he was almost œdema-free, chlorothiazide increased the natriuresis and induced a further loss of 6 lb. in the next 10 days, but the blood-urea rose from 50 mg. per 100 ml. on admission to 150 mg. No abnormality of the electrolytes was found; and as there was no dehydration (judged by the extracellular-fluid volume, which had fallen from 23·0 litres to a normal value of 15·4 litres), the azotæmia was attributed to a further deterioration in renal function.

The third patient (no. 14), who showed only a fair response, became œdema-free on chlorothiazide, but increased activity led to some reaccumulation of fluid.

Valvular heart-disease.—There were three patients in this group:

One (no. 15) responded well, losing 10 lb. in weight and becoming œdema-free.

A second (no. 16), who had been in chronic congestive failure for 3 years with frequent hospital admissions, was readmitted with gross œdema. Bi-weekly injections of mersalyl for 17 days produced no improvement, and he gained 3 lb. Chlorothiazide (2 g. daily for a week and then 3 g. daily for 10 days) caused only a 5 lb. loss of weight. The addition of mersalyl induced a further diuresis, and the weight fell another 10 lb. This result, which can only in part be attributed to chlorothiazide (although seemingly as a result of its use the patient became responsive to mersalyl), has been classified as fair. The third patient (no. 17) had been in failure for many months with mitral stenosis, aortic incompetence, tricuspid incompetence, and cardiac cirrhosis. No significant improvement followed treatment with chlorothiazide or mersalyl (with or without ammonium chloride) either singly or in combination.

Premenstrual œdema

All three patients responded well to chlorothiazide given 7–10 days before the onset of their menses, when symptoms were liable to start. The result in 1 of these patients is shown in fig. 4.

Cirrhosis

One patient with alcoholic cirrhosis, ascites, and œdema of the legs lost 7 lb. in 8 days. Treatment was stopped because she felt increasingly anorexic and unwell; but as no electrolyte abnormality was found, her symptoms were probaby more related to sudden withdrawal of alcohol than to chlorothiazide.

Nephrosis

This patient with chronic spinal tuberculosis had amyloid nephrosis, shown by finger-clubbing, hypoalbuminæmia, heavy proteinuria, and 75% retention of congo-red.

Chlorothiazide induced a striking diuresis and weight loss of 26 lb., the extracellular-fluid volume falling from 29·9 to 18·5 litres. Despite continuing hypoproteinæmia the patient was œdema-free, and the dose of chlorothiazide was reduced from 2 to 1 g. daily. Although he was on a high-protein diet containing 218 mEq. of sodium, hypokalæmia of 2·8 mEq. per litre developed, and a potassium supplement of 80 mEq. daily was given to correct this. The œdema returned and was not controlled until the dose of chlorothiazide was raised to 4 g. daily. Chlorothiazide did not increase the urinary concentration of protein, 40 g. daily being excreted during the diuretic phase.

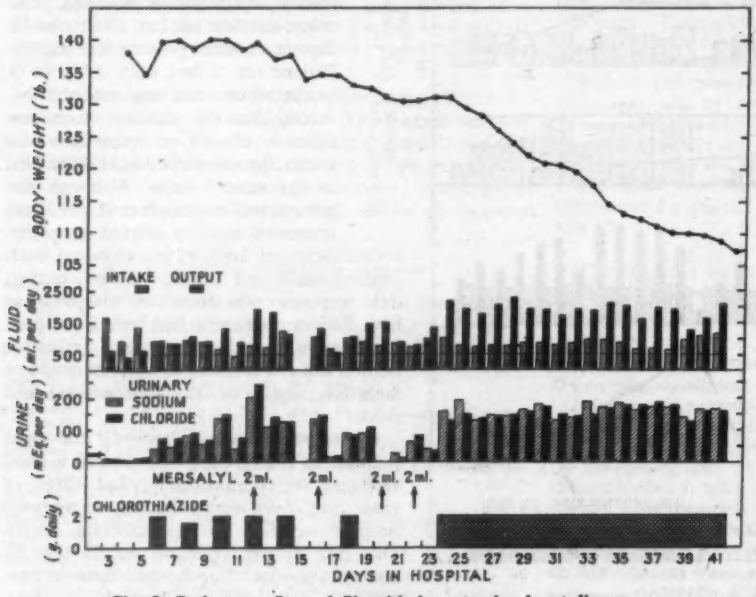

Fig. 3—Patient no. 7, aged 71, with hypertensive heart-disease.

The dietary sodium intake (22 mEq. daily) is shown by the arrow on the sodium and chloride scale. Note gradual increase in sodium and chloride excretion on days 6, 8, and 10 when chlorothiazide is given on alternate days. On day 12 the combination of mersalyl and chlorothiazide causes a further increase in the water and sodium diuresis. On day 22 there is a poor response to mersalyl alone and no weight loss. A good response follows 2 g. chlorothiazide daily started on day 24.

Miscellaneous

One patient (no. 23) with œdema of the legs and abdominal wall due to malignant obstruction of the inferior vena cava showed a good response and lost 13 lb. in 14 days. Another with cirrhosis (no. 24), who developed œdema after a portacaval anastomosis, was only fairly well controlled on chlorothiazide 1 g. given for 4 days each week, and became hypokalæmic.

Electrolyte Disturbances and Toxic Effects

On the intake of sodium chloride given to these patients no significant changes in serum

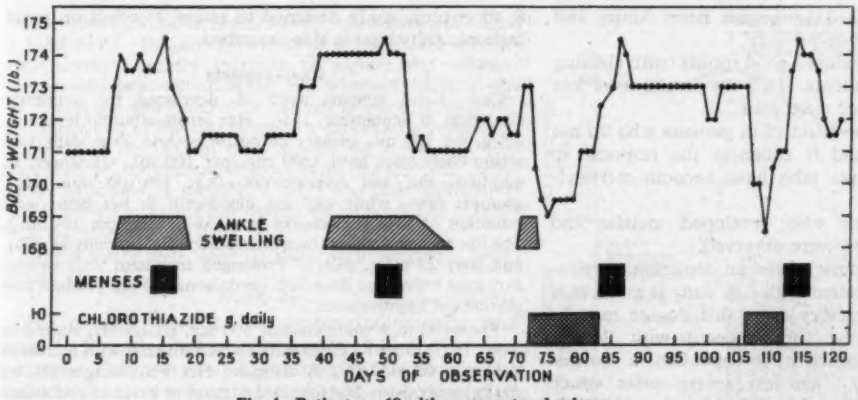

Fig. 4—Patient no. 18 with premenstrual œdema.

Chlorothiazide given before the third and fourth menstrual periods largely controls the symptoms and weight gain, but should have been continued during the menstruation.

sodium, chloride, or bicarbonate levels were observed, but the serum-potassium level tended to fall (as shown in fig. 2), and in all eleven patients whose urinary excretion of electrolytes was studied there was increased loss of potassium. In three patients the serum-potassium level dropped to below 3 mEq. per litre without symptoms of potassium depletion, and a fourth had such symptoms with a serum-potassium level of 3·1 mEq. Chlorothiazide was given daily to three of these patients, and for 4 days each week to the fourth. In two the daily intake of sodium was 22 mEq., in one it was 87 mEq., and in the fourth, with nephrosis and heavy proteinuria, it was 218 mEq.

No changes in liver-function tests, white-cell and platelet counts, or hæmoglobin levels were seen. None of the patients developed gastro-intestinal or other symptoms attributable to chlorothiazide, with the single possible exception of the cirrhotic patient (no. 21), who became anorexic and felt unwell.

Comparison with Mersalyl

A detailed comparison of the potency of chlorothiazide and mersalyl will be reported elsewhere. It will be seen, however, from table I and from fig. 2 that patients who responded poorly or not at all to bi-weekly injections of mersalyl may have a satisfactory diuresis on chlorothiazide.

Refractoriness to mersalyl, despite persisting œdema, may be due to the severity of the patient's condition, a low glomerular filtration-rate, or electrolyte imbalance (Stock et al. 1951). None of these eleven patients who responded poorly to mersalyl had hypochloræmic alkalosis, hyponatræmia, or hypokalæmia; yet five of them gave a good and four a fair response to chlorothiazide. Fig. 3, for example, shows little fall in weight on days 20 and 22, when mersalyl alone was given, but a good diuresis and weight loss when continuous chlorothiazide treatment was started on day 24.

Chlorothiazide and mersalyl given together produce a greater diuresis than either given alone. For example, in fig. 3 electrolyte and water excretion was greater on day 12, when the two agents were given together, than on days 6, 10, and 14, when chlorothiazide was given alone, or on days 16, 20, and 22, when mersalyl was given alone. Furthermore, chlorothiazide may increase the response to mersalyl in patients who have become mersalyl-resistant, if the two agents are given together (Bayliss et al. 1958). This enhanced response to combined treatment may be of clinical value in patients whose œdema fails to clear completely on chlorothiazide alone, and suggests that chlorothiazide and mersalyl may influence two different mechanisms for the tubular reabsorption of chloride.

Discussion

The ideal diuretic should (*a*) be effective by mouth, (*b*) be at least as potent as mersalyl, (*c*) cause a proportionate loss of sodium, chloride, and water, (*d*) not induce any electrolyte imbalance, (*e*) not lose its effectiveness (so that it can be given continuously if necessary and allow the seriously incapacitated patient to eat a diet containing a palatable amount of sodium chloride), and (*f*) be devoid of toxic effects. Such a substance does not exist, but chlorothiazide meets many of these desiderata. It is effective by mouth, causes almost equimolar loss of sodium and chloride, and in our experience has been outstandingly free from toxic effects. It may cause potassium depletion, and is not always therapeutically effective; but it would be difficult to imagine any substance that would unfailingly induce a diuresis in severe congestive cardiac failure, particularly when the glomerular filtration-rate is much reduced. Many of the cardiac patients who showed a poor or fair response to chlorothiazide were old, chronically ill, and resistant to other forms of treatment. Indeed it is more remarkable that several of this type (e.g., nos. 1, 5, 7, 8, and 16) responded to chlorothiazide at all.

Potassium depletion and hypokalæmia may develop during treatment with any diuretic that increases the excretion of chloride or bicarbonate, and the more potent the diuretic the more likely is this to happen. Usually the increased amount of chloride excreted will be accompanied by sodium; but, if the amount of available sodium is reduced—either because of rigid dietary restriction, or because of intense tubular reabsorption of sodium—potassium may be excreted instead. Our experience shows that continuous daily administration of 2 g. chlorothiazide may cause potassium depletion, and as daily treatment may be necessary for a long time in severely ill refractory patients, a careful watch should be kept on the serum-potassium level, and daily supplements of potassium chloride 2–6 g. in capsules should be given to prevent hypokalæmia. In less severe cases which respond quickly, continuous administration of chlorothiazide 2 g. daily is necessary for only a few days, and thereafter a smaller dose, 1·0–1·5 g. daily, can be used and maintenance therapy given intermittently on 3–4 days each week.

Summary

The value of chlorothiazide, a non-mercurial orally effective diuretic, has been assessed in 24 œdematous

patients, of whom 17 had congestive heart-failure and 11 had responded poorly to mersalyl.

A daily dose of 2 g. produced good results (with clearing of the œdema) in 14 patients. In 7 the results were less satisfactory, and in 3 they were poor.

Chlorothiazide may be effective in patients who do not respond to mersalyl, and it enhances the response to mersalyl even in patients who have become mersalyl-resistant.

Except for 1 patient who developed malaise and anorexia, no toxic effects were observed.

Chlorothiazide may cause potassium depletion, particularly if continuous treatment with 2 g. daily is given over a long period. In refractory cases this dosage may be required and should be supplemented with 2–6 g. potassium chloride (sufficient to maintain a normal serum-potassium level). In less severe cases which respond quickly a smaller dose of chlorothiazide (1·0–1·5 g. daily) may suffice; and for maintenance therapy the drug may be given intermittently on three or four days each week.

We are grateful to Drs. C. J. Gavey and F. Dudley Hart for allowing us to study patients under their care; to Miss Margaret Wood and Miss Jill Nuttall for technical assistance; and to Messrs. Merck Sharp & Dohme for generous supplies of chlorothiazide ('Saluric').

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CLINICAL EXPERIENCE WITH CHLOROTHIAZIDE

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CHLOROTHIAZIDE is a new oral non-mercurial diuretic. Chemically it is 6-chloro-7-sulphamyl-1,2,4-benzothiadiazine-1, 1-dioxide, a heterocyclic compound containing a sulphonamido group. Preliminary studies by Ford et al. (1957) have shown that it is as effective as the mercurial diuretics. In vitro it inhibits carbonic anhydrase but in vivo it causes a considerable increase in the rate of excretion of chloride and sodium without producing metabolic acidosis. The effect on chloride output is unlike the action of carbonic anhydrase inhibitors (Hanley and Platts 1956) and resembles the action of organic mercurial compounds.

We report here our initial clinical experience with chlorothiazide in three patients with the nephrotic syndrome, one patient with ascites due to portal hypertension, and one patient with congestive heart-failure. A short-term study designed to assess its effect on renal carbonic anhydrase is also described.

Case-reports

Case 1.—A woman, aged 38, developed the nephrotic syndrome in September, 1956. Her serum-albumin level was 1·8 g. per 100 ml., urinary output of protein 25 g. daily, and serum-cholesterol level 1300 mg. per 100 ml. However, in addition, she had hypertension (B.P. 190/100 mm. Hg), granular casts, white and red blood-cells in her urine, and retention of urea (blood-urea level 34–62 mg. per 100 ml.). She has been maintained on a low-sodium diet (initially 44 mEq. and later 22 mEq. daily). Prolonged treatment with cation-exchange resins and later with prednisone did not produce any permanent improvement.

Treatment with chlorothiazide 500 mg. six-hourly, started in May, 1957, caused a rapid well-marked diuresis with increased excretion of sodium and chloride. Her body-weight fell by 3·9 kg. in six days. She then had a transient attack of abdominal pain, diarrhœa, and vomiting. Chlorothiazide was withheld, and she lost 3·0 kg. Renewed administration of chlorothiazide (500 mg. twelve-hourly) ten days later did not cause gastro-intestinal symptoms, and she has now taken chlorothiazide intermittently—one week every alternate week—for six months without ill effect. Her weight has remained steady, and she feels well and is almost free from œdema. Persistent hypokalæmia has developed and is only partially controlled by an extra 40–80 mEq. of potassium daily (potassium chloride 3–6 g.). No clinical effects attributable to hypokalæmia can be recognised.

Case 2.—A woman, aged 49, developed the nephrotic syndrome in March, 1956. Her serum-albumin level was 1·7 g. per 100 ml., urinary output of protein 22 g. daily, and serum-cholesterol level 780 mg. per 100 ml. Her blood-pressure was normal. Her urine contained white blood-cells and a few red blood-cells but no casts, and her blood-urea level was normal. The œdema persisted despite treatment with a low-sodium diet (30 mEq. daily), prednisone, and mersalyl injections. Treatment with cation-exchange resin, started in September, 1956, was poorly tolerated but controlled the œdema. Resins were stopped in May, 1957, and her weight increased by 2·3 kg. in two weeks on a diet containing 22 mEq. of sodium daily.

Treatment with chlorothiazide 500 mg. six-hourly was begun in June, 1957. The patient lost 2·0 kg. in the next six days, with a prompt diuresis and increased excretion of sodium and chloride. Since then a maintenance dose of 500 mg. eight-hourly (given at first every alternate week and later for four days in each week) has controlled her œdema and body-weight. There has been a tendency to hypokalæmia, and despite an extra 55 mEq. of potassium daily the plasma-potassium level has on occasions fallen to 2·8 mEq. per litre.

Case 3.—A man, aged 37, developed the nephrotic syndrome in April, 1957. His urinary output of protein is 25 g. daily, serum-albumin level 1·2 g. per 100 ml., and serum-cholesterol level 890 mg. per 100 ml. He also has hypertension (B.P. 140/100 mm. Hg), retention of urea (blood-urea level 103 mg. per 100 ml.), and numerous granular casts and white and red blood-cells in his urine. There had been little response to a low-salt diet and prednisone therapy.

Treatment with chlorothiazide began after a control period on a low-sodium diet (22 mEq. daily). 500 mg. six-hourly, begun in October, 1957, caused a prompt diuresis, increased urinary excretion of sodium and chloride, and a weight loss of 4·6 kg. in eleven days. The intake of sodium was subsequently increased; but, when it exceeded 44 mEq. daily, œdema reappeared.

Case 4.—A man, aged 69, developed ascites due to portal hypertension and diffuse hepatic fibrosis in August, 1955. The ascites was controlled successfully for the first sixteen months with a low-sodium diet (22 mEq. daily) and weekly mersalyl injections, but over the next five months more ascitic fluid developed despite twice-weekly mersalyl injections.

Treatment with chlorothiazide 500 mg. six-hourly was started in June, 1957. Initially this provoked a considerable diuresis with increased urinary excretion of sodium and chloride. Two months later chlorothiazide had become ineffective, and the patient was also found to be resistant to mersalyl injections. A combination of the two treatments produced a satisfactory diuresis, and for the past three months the ascites has been controlled by continuous chlorothiazide therapy with twice-weekly injections of mersalyl 2 ml. The plasma-potassium level is 3·0–4·1 mEq. per litre despite 6 g. of potassium chloride (80 mEq. of potassium) daily.

Case 5 was a man, aged 80 years, with congestive heart-failure.

Methods

The patients were studied in hospital initially, and cases 1, 2, and 4 were subsequently followed as out-patients. They were intelligent, cooperative people who could be relied on to keep to their diets and to collect their urine accurately. Before chlorothiazide was given, there was a control period of 4–8 days on a diet of fixed sodium and chloride content. Blood-pressure and body-weight were recorded daily. Twenty-four-hour collections of urine were made, and their accuracy checked by creatinine estimations. Electrolyte and protein levels in the plasma and in the urine were determined by standard laboratory methods, and urinary glucose by the glucose-oxidase technique of Froesch and Renold (1956). In the short-term study the urine was collected by catheter, and both urine and arterial blood were kept from contact with air. The pH was estimated within 10 minutes of collection at 37°C on the pH meter described by Wynn and Ludbrook (1957). A Stadie electrode system was used and standardised with fresh phthallate buffer at pH 4·025. Titratable acidity was estimated by titration with standard NaOH to pH 7·4.

Results

Short-term Study

The patient selected for this had rheumatic heart-disease and benign essential hypertension. She had had

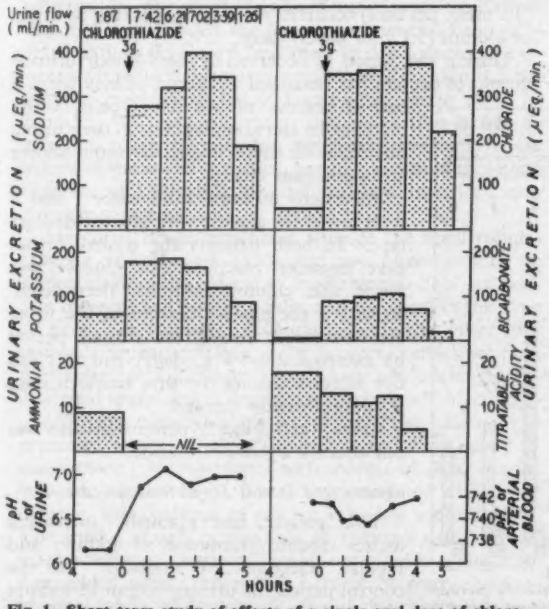

Fig. 1—Short-term study of effects of a single oral dose of chlorothiazide 3 g. on pH of arterial blood and on volume and composition of urine.

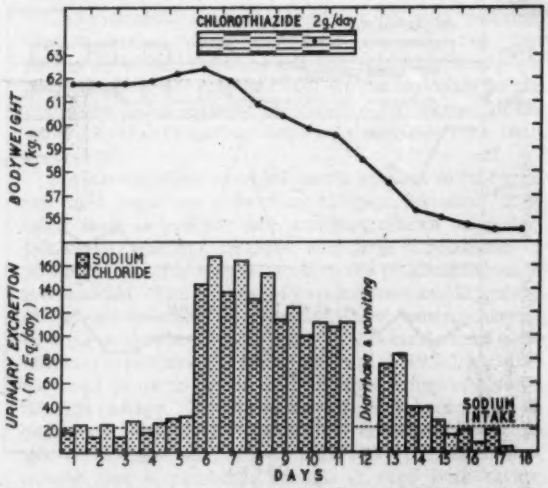

Fig. 2—Case 1 (nephrotic syndrome): effect of initial course of chlorothiazide on body-weight and urinary excretion of sodium and chloride.

congestive heart-failure, but this had responded to rest in bed, a low-sodium diet, and digitalis. She was able to concentrate the urine to sp. gr. 1·027, and her blood-urea level was 30 mg. per 100 ml. Twelve hours after the last meal control samples of arterial blood and urine were obtained. Chlorothiazide 3 g. (53 mg. per kg. of body-weight) was then given by mouth, and changes in her blood and urine were followed for the next five hours. The patient remained fasting but was encouraged to drink tap-water. The results are shown in fig. 1. There was a slight but definite transient decrease in the pH of her arterial blood, an increase in the pH of her urine, and a sharp rise in the rate of excretion of bicarbonate. The rate of excretion of hydrogen-ion diminished (decrease in titratable acid and disappearance of ammonia), and the rate of

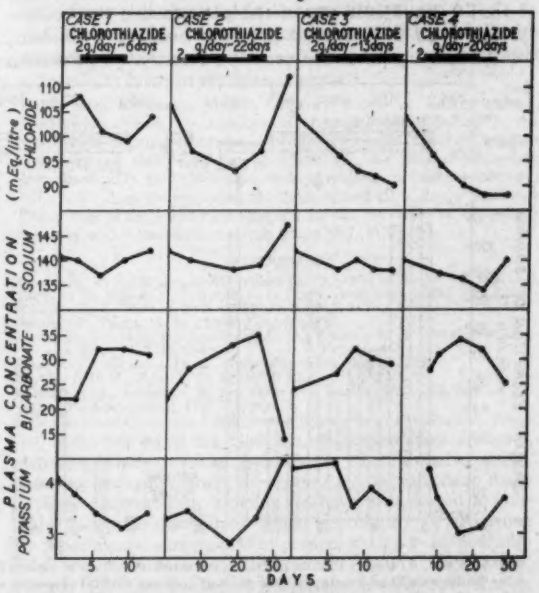

Fig. 3—Plasma-electrolyte levels during initial period of treatment (cases 1-4).

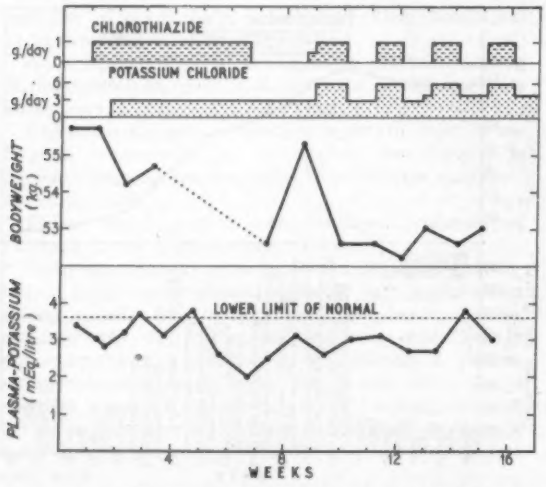

Fig. 4—Case 1 (nephrotic syndrome): effect of prolonged intermittent chlorothiazide therapy on body-weight and plasma-potassium level.

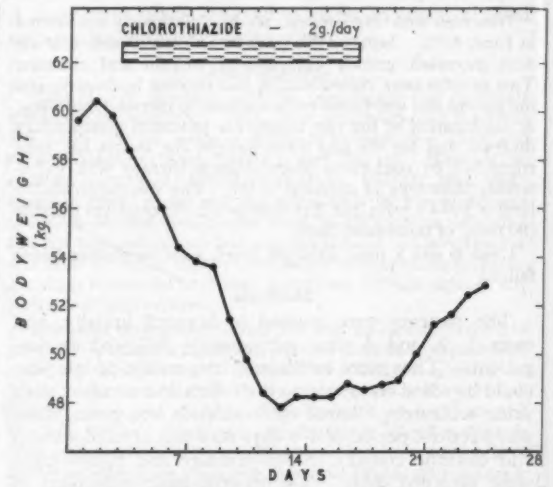

Fig. 6—Case 5 (congestive heart-failure): response of body-weight to first course of chlorothiazide.

excretion of potassium increased about three-fold. These effects can reasonably be attributed to inhibition of renal carbonic anhydrase (Counihan et al. 1954). The considerable increase in excretion of chloride is unlike the effects of carbonic anhydrase inhibitors and suggests that chlorothiazide has a separate action similar to that of the organic mercurial diuretics.

Nephrotic Syndrome (cases 1–3)

Before receiving chlorothiazide all three patients were œdematous and retaining sodium despite a very low intake. When chlorothiazide was given, they had a prompt diuresis with loss of weight and reduction or disappearance of œdema. There was a considerable increase in the urinary excretion of sodium and chloride, the average ratio of chloride to sodium in the first six days being 1·18:1·0 (fig. 2). In two of the patients this was accompanied by 25–33% increase in urinary output of potassium; in the third patient the urinary excretion of potassium decreased slightly during the first five days but increased later to an average of 27% above the control levels. Changes in plasma-electrolyte levels are shown in fig. 3.

Cases 1 and 2 have now been on treatment with a low-sodium diet and intermittent chlorothiazide for five or six months. Œdema is controlled, and the patients feel well, but both have developed persistent hypokalæmia despite oral potassium supplements of up to 80 mEq. daily as potassium chloride (fig. 4). Studies with an increased sodium diet were made on case 3 in hospital. When taking chlorothiazide he could be allowed 44 mEq. of sodium daily; but, if the intake was increased to 88 mEq. daily, œdema returned. It had been hoped that a diet with a higher sodium content would reduce the tendency to hypokalæmia, but the lowest plasma-potassium level (3·1 mEq. per litre) occurred while he was having 88 mEq. of sodium (5·1 g. of NaCl) daily.

During the period of observation the 24-hour urinary output of protein has remained unaltered. Cases 1 and 3 had an excess of red blood-cells, white blood-cells, and granular casts in their urine, but repeated Addis counts have not shown any significant change.

Specimens of urine from cases 1 and 2 were tested for glucose with glucose-oxidase tape. In both patients the control urines gave negative reactions but glucose was found after chlorothiazide had been given. In case 3 the glucose content of the urine was measured; during the control period he excreted 2·9–3·9 g. daily, and this did not increase during the first fourteen days of chlorothiazide therapy.

Cases 1 and 3 had hypertension; this was not affected by chlorothiazide.

Ascites and Portal Hypertension (case 4)

This patient had gradually increasing ascites despite restriction of sodium and regular injections of mersalyl. In the control period his urinary output of sodium was 1–2 mEq. daily; given chlorothiazide he had at first a prompt diuresis with a

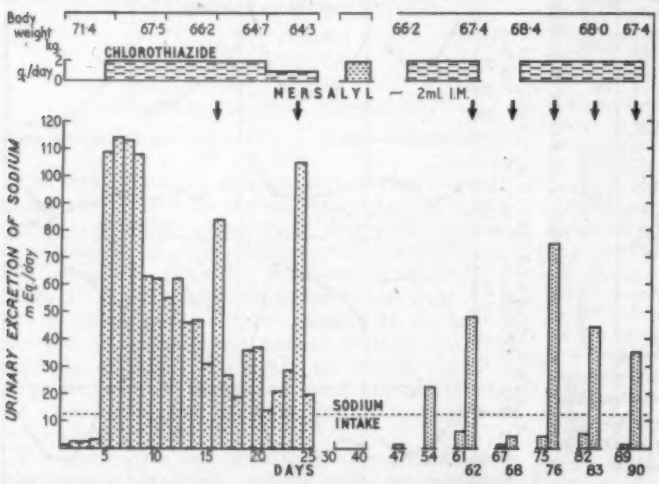

Fig. 5—Case 4 (ascites due to portal hypertension): effect of chlorothiazide therapy on body-weight and urinary excretion of sodium. Initial response was satisfactory, but after seven weeks patient became resistant to chlorothiazide and mersalyl given separately, although he responded when they were given together.

considerably increased output of sodium and chloride. The average urinary chloride to sodium ratio over the first six days was 1·50: 1. During the initial eleven days of treatment losses of potassium exceeded the estimated intake by about 330 mEq., and at the end of this time the plasma-potassium level had fallen to 3·0 mEq. per litre. Subsequent details of this patient are shown in fig. 5. He has become refractory to the action of chlorothiazide and to that of mersalyl although he still responds when both drugs are given together. Resistant hypokalæmia has developed, but no symptoms can be attributed to it.

Congestive Heart-failure

Fig. 6 illustrates the dramatic response obtained with chlorothiazide in an old man with congestive heart-failure. Rest in bed, a low-sodium diet, and digitalis had not relieved his breathlessness and œdema. When he was given chlorothiazide, his general condition and appetite improved; but it was impossible to keep him to a low-sodium diet. A steady state was finally achieved with a normal diet without added salt, chlorothiazide 2 g. daily, and injections of mersalyl 2 ml. twice a week. His plasma-potassium level fell to 3·4 mEq. per litre, and in a second patient with heart-disease the plasma-potassium level fell to 3·0 mEq. per litre after 9 g. of chlorothiazide had been given for four days.

Discussion

The chief action of chlorothiazide appears to be to cause a rapid increase in the rate of excretion of chloride by the kidneys. In this it resembles closely the diuretic action of organic mercurial compounds (Pitts and Sartorius 1950). A different effect, attributable to the inhibition of carbonic anhydrase, can be demonstrated in short-term studies. This secondary action may explain why chlorothiazide produces considerable hypokalæmia, although it is unusual for mercurial diuretics to do so.

In practice chlorothiazide has proved to be a most effective diuretic agent. In two of our patients the diuretic action has continued for five or six months, although a third patient developed resistance in two months. Compared with injections of mercurial diuretics, chlorothiazide has the great advantage of being active when taken by mouth. We have no reason to believe that it will be effective given to patients completely resistant to the action of mercurial diuretics, but in this situation a combination of chlorothiazide and mersalyl injections may provoke a diuresis.

Mercurial drugs sometimes damage the renal tubules (Preedy and Russell 1953) and are often avoided in patients with renal œdema. Chlorothiazide does not contain mercury and may be a safer diuretic agent in this type of case. It compares favourably with the other oral diuretic drugs available. It is more effective than acetazolamide (' Diamox ') and does not cause gastro-intestinal symptoms as does aminometradine (' Mictine ').

Although chlorothiazide is an effective diuretic, a restricted intake of salt will continue to be necessary in many cases. Most patients with œdema of renal origin, or with ascites from portal hypertension and liver damage, will continue to require very low sodium diets. The intake of salt permissible in patients with cardiac œdema will vary; some will be able to tolerate a diet with " no added salt "; others will have to be restricted to a minimal intake of dietary salt despite the continuous use of chlorothiazide.

Chlorothiazide seems to be remarkably well tolerated. Gastrointestinal disturbances are unusual; our first patient developed diarrhœa and vomiting when first given chlorothiazide but she had had similar episodes in the past when losing œdema fluid rapidly. No changes of the white blood-cells and no sensitivity reactions have been observed.

The development of hypokalæmia appears to be by far the most important side-effect of chlorothiazide. It is most likely in patients with resistant œdema on a low-salt intake; and, in such cases, even large supplements of potassium chloride may fail to keep the plasma-potassium level normal. The dangers of hypokalæmia are difficult to assess. We have not met with any clinical features that can be attributed to it. Hypokalæmia may potentiate the toxic effects of digitalis on the heart (Lown et al. 1951), and this may well prove to be the most serious danger of chlorothiazide therapy. The possibility of renal damage due to prolonged depletion of potassium should also be considered (Relman and Schwartz 1956). If a patient has œdema that is persistent enough to need both severe restriction of sodium (44 mEq. or less daily) and chlorothiazide therapy (either continuous or intermittent), we would regard it as essential to have regular estimations of plasma-potassium concentrations. Initially these should be made at weekly intervals, and suitable supplements of potassium chloride should be given.

Summary

A new oral non-mercurial diuretic, chlorothiazide, has been used successfully in patients with the nephrotic syndrome, ascites due to portal hypertension, and congestive heart-failure. Two patients with the nephrotic syndrome have now been controlled satisfactorily for five or six months.

Chlorothiazide therapy was followed by a considerable and prompt diuresis, with increased excretion of sodium and chloride. The mode of action and the therapeutic response resemble those of the mercurial diuretics. A subsidiary effect suggesting inhibition of carbonic anhydrase was observed in a short-term study.

Chlorothiazide caused hypokalæmia which was difficult to control with oral potassium supplements. No other side-effects have so far been observed.

We wish to thank Messrs. Merck, Sharp & Dohme, Ltd., Hoddesdon, Herts, for supplies of chlorothiazide (" Saluric "); the staff of the routine laboratories of the Courtauld Institute of Biochemistry of the Middlesex Hospital for the plasma-electrolyte estimations; Dr. E. K. Westlake for help with the pH determinations; Mr. V. K. Asta for preparing the figures; and the Clinical Research Committee of the Middlesex Hospital for the provision of laboratory facilities and a personal research grant to J. D. N. N.

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" Time was when the clinician could encompass anatomy, physiology and experimental medicine. These days have gone. Anatomy and physiology, as separate disciplines, have made fantastic progress and, in doing so, have been forced to subdivide into other disciplines. Might not the time be opportune for experimental surgery also to prepare itself for the next step in its evolution as a medical science? "—W. J. DEMPSTER, F.R.C.S., *An Introduction to Experimental Surgical Studies*, p. 14. Oxford, 1957.

CONTROL OF TREATMENT IN MYXŒDEMA BY ELECTROCARDIOGRAPHY

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The recognition of cardiac symptoms in cases of myxœdema that have gone for long periods without treatment is of great practical importance, for when heart disease is present treatment with thyroid extract must be carried out with great care.—G. R. MURRAY, 1897.

THIS warning, issued at the outset of thyroid treatment for myxœdema, has been fully justified in the experience of the past sixty years but is still largely ignored. It is the purpose of this paper to define the danger of indiscriminate dosage and to show the value of electrocardiography in controlling treatment.

It must be assumed that every patient with obvious myxœdema has heart-disease, either from atheroma or from the involvement of the myocardium in the disease itself; hence every patient is in danger from careless treatment. Brewer (1951) notes the extreme scarcity of necropsy reports on untreated cases of myxœdema and thinks this is due to the introduction of thyroid treatment in 1891. I doubt if this really explains it, for I am convinced that untreated myxœdema still abounds. The twelve cases I am recording represent less than half of the patients I have treated during the past ten years. These twelve were typical and recognisable at sight, yet only three had had any previous treatment. One of them was interesting in this respect because, although the clinical picture was typical and recognisable, it was not recognised, even in hospital, until the electrocardiogram pointed the way. It showed how easily even a typical case may escape recognition unless this possibility is constantly borne in mind.

Necropsy records of treated cases, though not plentiful, are readily found. Brewer (1951) recorded one, and Smyth (1938) collected five from American literature and records one of his own. In every case death was due to acute coronary insufficiency attributed to treatment with thyroid. If untreated myxœdema is as prevalent as it seems to be and necropsy records are only to be found in treated cases, it suggests that treatment can be more deadly than the disease.

A great difficulty in selecting safe and adequate dosage has been the lack of a reliable means of assessing adequacy. Zondek (1918) recorded the typical electrocardiographic changes in myxœdema; but, I believe, this observation has not come into regular use for controlling treatment. This method of control was used in all my cases.

The twelve patients in this series all attended my clinic at Torbay Hospital in 1945-57. Only those with a significantly lowered basal metabolic rate (B.M.R.) are included. The year of their first visit is noted with their ages in table I. Every patient was seen for final assessment in 1957.

TABLE I—DOSAGE OF THYROID (GRAINS)

Case no.	Sex	Date	Age (yr.)	B.M.R. (%) *	Previous thyroid treatment	Daily dose (grains)		Final assessment	
						A	B	Health	Dose
1	M	1947	43	−30	None	1½	2	Good	2
2	F	1954	70	−31	None	1½–6	1	Hypothyroid	1
3	M	1952	48	−6	None	¼	½	Very good	½
4	M	1950	55	−37	None	2–½	1½	Fair	1
5	M	1945	56	−25	None for 6 weeks	½	1	Fair	1
6	F	1955	54	−3	None	¼	1½	Fair	1
7	F	1948	51	−11	None	½	2	Good	1½
8	F	1937	31	−15	None for 10 years	2	1½	Fair	2
9	F	1950	38	−28	None for 3 months	½	1½	Fair	1½
10	F	1954	50	−44	None	¼	1½	Very good	1½
11	F	1951	36	−30	None	½	1	Very good	1
12	F	1951	38	−18	None	¼	1	Good	1½

* Before treatment. A, Inital. B, Maintenance.

Electrocardiograms.—To simplify the evidence only the standard limb leads are recorded. The characteristic feature in myxœdema is flattening or inversion of the T waves in all leads and their rise in response to treatment with thyroid. The T-voltage changes are recorded in table II.

Dosage.—Throughout this paper only the daily total of thyroid extract in grains is noted. The initial and maintenance doses in each case are recorded in table I.

Case-reports

Case 1.—A man, aged 43, was admitted to hospital on Nov. 15, 1947, with painful swellings of his arms, thought to be cellulitis.

TABLE II—ANALYSIS OF T-WAVE VOLTAGE IN (MILLIMETRES)

Case no.	A			B			C			Dates
	T_1	T_2	T_3	T_1	T_2	T_3	T_1	T_2	T_3	
1	−2·5	−2·5	−1	+2	+2·5	+1	+3·5	+5	+2	A Nov. 17, 1947 B Dec. 24, 1947 C Mar. 3, 1948
2	+1·5	−3·5	−4·5	+1	−1	−2·5	+1	+	+1	A Oct. 29, 1954 B Feb. 4, 1955 C May 1, 1957
3	+2	+1	−1·5	+3	+4·5	+1·5	+2·5	+2·5	+1	A Aug. 29, 1952 B Nov. 7, 1952 C Feb. 1, 1957
4	−1·5	+1·5	+2·5	−2	±	0	−3·5	+1·5	+5·5	A Mar. 11, 1950 B Sept. 28, 1950 C Jan. 31, 1957
5	+2	−	−3	+3	+	−3	+4	+2	−3	A Nov. 24, 1945 B Jan. 11, 1946 C Aug. 2, 1947
6	−1	−3·5	−1	0	+2	+1·5	0	+1·5	+	A April 3, 1956 B Jan. 30, 1957 C June 11, 1957
7	+1·5	+	±	+2·5	+1·5	−	+2·5	+2	−	A Dec. 18, 1953 B June 15, 1954 C Feb. 6, 1957
8	+1	+2	+	+5	+2·5	−2	+2	+3·5	+1	A July 22, 1950 B Sept. 2, 1950 C May 29, 1951
9	+	+2·5	+2	0	+1·5	+1·5	+	+3·5	+3	A Oct. 2, 1950 B Jan. 31, 1951 C Mar. 5, 1957
10	−	0	+	+1·5	+2	+1	+4	+4	+	A June 24, 1954 B Oct. 9, 1954 C Jan. 11, 1957
11	+	0	−	+	+2·5	+2	+3	+4	+1	A Dec. 15, 1950 B Mar. 16, 1951 C Jan. 18, 1957
12	0	−	−	+1·5	+1	−1	+1·5	+	−1·5	A May 14, 1953 B Nov. 26, 1953 C Mar. 12, 1957

A, before treatment, except in case 3. B, first significant voltage change. C, final state. $\left.\begin{matrix}-\\+\end{matrix}\right\}$ less than 1 mm. 0, isoelectric.

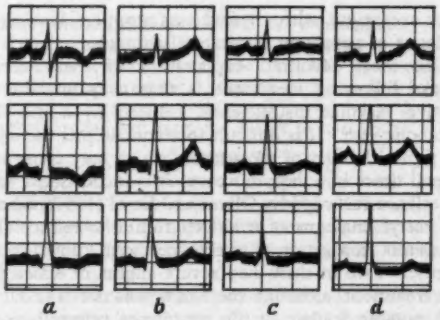

Fig. 1—Serial electrocardiograms of case 1: *a*, Nov. 17, 1947: *b*, March 3, 1948: *c*, Jan. 25, 1957: *d*, April 11, 1957.

He had had some chest pain on exertion; so an electrocardiogram was taken (fig. 1*a*). It suggested myxœdema, and in the light of this the clinical picture was seen to be typical. The patient was started at once on thyroid gr. 1, gradually increased to gr. 2 by Jan. 7, 1948. The swellings quickly subsided, and by March 3, 1948, the T voltage was fully restored (fig. 1*b*). The patient was not seen again for 10 years, when he was sent for on Jan. 25, 1957. The painful swellings of his arms had returned, he complained of feeling cold and breathless, and T voltage was reduced (fig. 1*c*). He said that 5 years previously the dosage of thyroid was reduced to gr. 1 daily because of palpitation. He had taken this dose since. It was now increased to gr. $1^1/_2$, and by April 11, 1957, his arms were normal and T voltage increased (fig. 1*d*). He still felt cold and breathless; so the original maintenance dosage of gr. 2 daily was restored. He has kept well on this since. It was remarkable how closely the rise and fall of the T waves corresponded to the disappearance and reappearance of localised patches of myxœdema.

Case 2.—A woman, aged 70, was admitted to hospital on Aug. 30, 1954, during my absence, with advanced myxœdema. She was at once given thyroid gr. $1^1/_2$ daily. After 10 days this dosage was increased to gr. $4^1/_{25}$ though she had already begun to complain of anginal pain, which she had never had before. On Sept. 22, 1954, the dosage was increased to gr. 6 daily. Next day the patient had an attack clinically resembling coronary thrombosis. The dosage was reduced to gr. 3 daily, and on Sept. 28, 1954, treatment with thyroid was stopped. On Oct. 4, 1954, the patient was still having angina at rest, but there were no signs of heart-failure. The electrocardiogram (fig. 2*a*) showed T inversion in all leads superimposed on the changes of myocardial ischæmia. Treatment with thyroid gr. $^1/_4$ daily was started, and increased to gr. $^1/_2$ on Oct. 11, 1954. She tolerated this, but an electrocardiogram taken 3 weeks later (fig. 2*b*) showed that it was inadequate. She kept on this dose for about a year, and it was then increased to gr. 1 daily. She was comfortable with this dose but could not tolerate gr. $1^1/_2$ daily; so gr. 1 daily was accepted as her maintenance dosage as an inevitable compromise. With this she kept reasonably well and could do all that she wanted to. When seen again on March 4, 1957, she was obviously hypothyroid, and electrocardiography still showed the typical T inversion (fig. 2*c*); but, when the dosage was increased to gr. $1^1/_2$ daily, she got more pain. She is still taking gr. 1 daily.

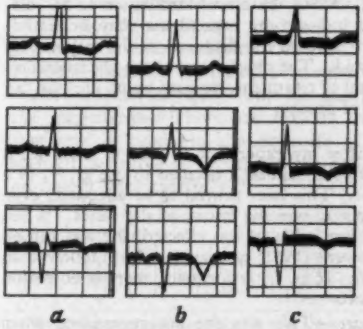

Fig. 2—Serial electrocardiograms of case 2: *a*, Oct. 4, 1954: *b*, Oct. 29, 1954: *c*, March 4, 1957.

Case 3.—A man, aged 43, underwent in 1947 partial thyroidectomy for thyrotoxicosis with auricular fibrillation. After operation normal rhythm was restored, and he was soon leading a very active life as a fruit farmer. At the age of 48 he came to see me on Aug. 28, 1952, because for the past 2 years he had become increasingly tired and had had three prolonged attacks of tachycardia with general trembling and lately he had been having chest pain on exertion. He said that during the past six months he had lost a stone in weight. Clinical examination revealed nothing of interest, and his electrocardiogram (fig. 3*a*) was passably normal. Further investigation revealed that his B.M.R. was −6%, basal pulse-rate 56, basal blood-pressure 112/88 mm. Hg, and blood-cholesterol level 235 mg. per 100 ml. On Sept. 14, 1952, he was started on thyroid gr. $^1/_4$ daily, and by Nov. 7, 1952, his electrocardiogram (fig. 3*b*) showed a striking rise in T voltage. The same dosage was continued, but 2 months later he began to feel tired again, and so it was increased to gr. $^1/_2$ daily. He has kept quite well on this dosage, doing exceptionally heavy work at times. This case shows that a single electrocardiogram may be misleading. It was the response of the T waves to thyroid that was pathognomonic.

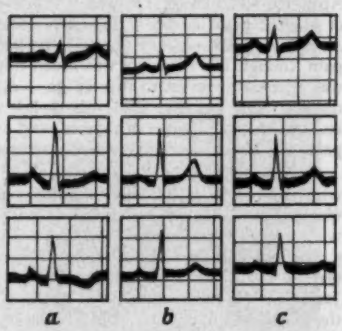

Fig. 3—Serial electrocardiograms of case 3: *a*, Aug. 28, 1952: *b*, Nov. 7, 1952: *c*, Feb. 1, 1957.

Case 4.—A man, aged 55, was admitted to hospital on March 27, 1950, with advanced myxœdema and a grossly enlarged heart T.T.D. 17·5 cm. He was started at once on thyroid extract gr. 2 daily. 8 days later he had an alarming attack of acute pulmonary œdema. The dosage of thyroid was reduced to gr. $^1/_2$ daily, and he promptly recovered. On May 26, 1950, he was much better, and the size of his heart was normal (total transverse diameter 12·5 cm.). The dosage of thyroid was increased to gr. 1 daily and 4 months later to gr. $1^1/_2$ daily. He kept on this dosage for 6 years. During this period he had a series of "thrombotic" events, left quadrantic blindness (April 27, 1950), right hemiplegia with aphasia (July 12, 1953), and acute coronary insufficiency (Dec. 25, 1956). The coronary attack was short and sharp, with complete recovery after 24 hours. The patient was kept in bed for 2 weeks but was afebrile and symptomless. The electrocardiograms were obscured by extreme left axis-deviation which persisted after the heart size was restored to normal. The day after the coronary attack there was slight R-T deviation in lead 4. The patient has had no anginal pain since and no residual heart weakness. After the coronary attack the dosage of thyroid was reduced to gr. 1 daily. The patient has kept well on this since.

Case 5.—A man, aged 56, who had been under treatment for progressive osteo-arthritis since 1933, begin to have angina of effort in February, 1945. In the following September myxœdema was discovered, and he was given thyroid gr. 3 daily. His anginal pain became worse and now came on at rest; sometimes he had three or four attacks a day. About a month after starting treatment with thyroid he had an attack considered to be coronary thrombosis, but no electrocardiogram was taken. Thyroid was stopped, and the pain then lessened, but during the next 6 weeks the patient became progressively more myxœdematous. On Nov. 24, 1945, he was admitted to Torbay Hospital, obviously myxœdematous. His B.M.R. was

—25%, and his electrocardiogram showed left axis-deviation with flattening of T_1 and inversion of T_2. He was still having angina of effort. On Dec. 20, 1945, treatment with thyroid gr. $^1/_2$ was started. He improved steadily and on Feb. 22, 1946, was having no serious pain, but his electrocardiogram 2 weeks later showed little change. The dosage of thyroid was increased to gr. 1 daily, which he tolerated quite well. Because of distortion by left axis-deviation the electrocardiogram was difficult to interpret; so on April 22, 1946, his B.M.R. was estimated again, and found to be —16%. The dosage of thyroid was gradually increased to gr. 2 by Jan. 4, 1947. On April 19, 1947, the B.M.R. was +7%, but he was having a lot of anginal pain; so the dosage was reduced to gr. $1^1/_2$ daily. At his last visit, on Aug. 2, 1947, he was still complaining of pain, though the T voltage was much improved (table II). He was advised to revert to thyroid gr. 1 daily. He then left the district. On Jan. 21, 1957, his doctor reported that he was still on the same dosage of thyroid, and was getting some effort pain, but his chief trouble was the arthritis.

Case 6—This case illustrates a special risk from overdosage with thyroid in myxœdema secondary to thyroidectomy. A woman, aged 54, was admitted to hospital on Jan. 9, 1956, with a large toxic goitre. She had been fibrillating for about a year but had no obvious signs of heart-failure. Her B.M.R. was +43%. She underwent complete thyroidectomy on Jan. 17, 1956, followed by a full course of radiotherapy because the goitre was malignant. On March 28, 1956, her appearance and behaviour suggested myxœdema; her B.M.R. was —3%, and her electrocardiogram showed inversion of T in all leads. Treatment with thyroid gr. $^1/_4$ daily was started on April 2, 1956, and increased to gr. $^1/_2$ daily on Aug. 29, 1956. Her principal symptom was depression, which was improving slowly but steadily. On Oct. 31, 1956, the dosage of thyroid was increased to gr. 1 daily. 3 months later the depression had passed and the electrocardiogram showed considerable improvement in T voltage, but the P–R conduction time was 0·24 sec., and the patient felt cold and was breathless on hills. The dosage of thyroid was increased to gr. $1^1/_2$ daily and a month later to gr. 2 daily. 2 months later she felt well but was fibrillating. Treatment with thyroid was stopped, and quinidine was given, which converted the fibrillation to flutter. In spite of full digitalisation, which induced nausea and vomiting, the flutter persisted, though at a slower ventricular rate. It seemed likely that the myocardium was damaged; so it was decided to let the flutter be and to control the ventricular rate with minimal doses of digitalis. In retrospect one can see that it would have been wiser to keep the thyroid dosage at gr. 1 daily, but at the time I thought her thyroid had been so thoroughly destroyed that she might need a larger dose than usual.

Discussion

Sensitivity to Thyroid

It is known that patients with myxœdema are apt to be hypersensitive to thyroid extract; the more advanced the disease the greater is this tendency. This sensitivity is expressed as anginal pain. In the angina of myxœdema the pattern of pain may be confused by treatment. Before treatment it usually appears as an effort pain, which subsides as treatment becomes effective. After treatment there may be added a pain with distinctive qualities which is aggravated by treatment. Seven of my patients had angina of effort relieved by treatment. Two of them (cases 2 and 5), after treatment had started, had spasms of pain at rest, sometimes three or four attacks a day, usually of short duration but sometimes lasting several hours. This pain was not relieved by trinitrin and was aggravated by thyroid. Both of these patients had started with grossly excessive dosage, and both of them had attacks indistinguishable clinically from coronary thrombosis. But in these attacks, though the pain was severe, collapse was minimal, and the attacks subsided quickly when treatment with thyroid was stopped, leaving little evidence of persistent myocardial damage.

The most favoured explanation of these coronary attacks following treatment is that they are due to a relative vascular insufficiency induced by a rise in the metabolic rate. It is difficult to reconcile this theory with the typical lability of the attacks, which may come and go several times in a day; moreover it is inconsistent with an experience recorded by Oliver and Boyd (1957), who used the acetyl analogue of triiodothyronine to reduce cholesterinæmia in a group of twelve men with known coronary disease. Two of them had severe angina of effort during this treatment, although the B.M.R. was not raised.

A notable feature in the necropsies referred to above was myocardial infarction without thrombosis. Brewer's (1951) patient died suddenly in a manner suggesting coronary thrombosis, but no thrombus was found. Smyth (1938) records a case in which a large area of necrosis was found in the myocardium without any evidence of thrombosis. He also says that, in three of the five other necropsies reviewed by him, on patients who had met a coronary death while under treatment, no thrombus was found. Wood (1956) refers to myocardial infarction without thrombosis as occurring in myxœdema when treated too vigorously with thyroxine. If these anginal crises and sudden deaths under treatment are sensitivity reactions, this could explain the capricious nature of the angina and infarction without thrombosis, because one can readily associate such coronary sensitivity with reversible occlusion in terms of intimal swelling and vasospasm.

The Electrocardiograms

On the whole the behaviour of the T wave fulfilled expectation. When the electrocardiogram is distorted by coronary disease, as in case 2, or by extreme axis-deviation, as in cases 4 and 5, it is not easy at first to recognise the T-wave changes of myxœdema, but in serial electrocardiograms these were recognisable in all cases. When the electrocardiogram is not distorted, the changes induced by myxœdema may be pathognomonic, but what clinches the diagnosis is the response of the T-waves to thyroid. The chief value of the electrocardiogram is in the control of treatment, because by its use one can judge the adequacy of dosage.

Dosage of Thyroid

Initial dosage.—After my experience in case 4, when gr. 2 induced acute ventricular failure, I decided to use gr. $^1/_4$ as a standard initial dose. This later proved to be adequate, even in case 10, whose B.M.R. was the lowest of the series. When the change in T voltage (table II) was effected, she was still on gr. $^1/_4$ daily. In Brewer's (1951) case sudden death followed an initial dose of gr. $^3/_4$. If gr. $^1/_4$ is adequate, there is no reason for starting with more.

Maintenance dosage.—This was the dosage reached when symptoms had cleared and T voltage was fully restored. From these results it seems to be rarely necessary to give more than gr. 2 daily for maintenance. In this series the thyroid needs bore no relation to the B.M.R. In case 10, with the lowest B.M.R., the maintenance dosage was only gr. $^1/_2$ whereas in case 8, in which the B.M.R. was only —15%, gr. 2 daily was needed to keep her free from symptoms.

Final Assessment

Every patient was re-examined in 1957. Three of them were hypothyroid. In two of these (cases 1 and 9) the maintenance dosage had been reduced; both of them improved promptly when the original maintenance dosage was restored. The other patient (case 2) cannot tolerate an adequate dosage and is still hypothyroid. The prominent symptoms in these hypothyroid cases was feeling cold and breathlessness. This cold feeling was a well-defined symptom; the patients never felt warm, even in bed: it is usually an early symptom and is the last to go. Breathlessness was prominent in most of the patients before

treatment; in four of these anæmia was a contributory cause, one of them (case 9) had heart-block. Breathlessness cleared up completely in all but three (cases 2, 6, and 9), all of whom had persistent heart damage. Anginal pain occurred in seven patients before treatment; it persisted in two (cases 2 and 5), both of whom had had excessive dosage to start with.

Summary

The reality of the danger of overdosage with thyroid in the treatment of myxœdema is amply confirmed.

Three of twelve patients had alarming heart-attacks attributable to treatment, and two of these remained intolerant to thyroid.

Some evidence suggests that these reactions may be true sensitisation reactions, which could be avoided by careful control of treatment—the electrocardiogram is a valuable help in this.

In myxœdema the initial dosage of thyroid should never exceed gr. $^1/_4$ daily, and thereafter the gradient of dosage should be controlled by serial electrocardiography.

The maintenance dosage must be assessed individually. None of my patients required more than gr. 2 daily, and most of them did well on less.

I have much pleasure in acknowledging my indebtedness to Dr. Cameron Davidson, who did all the B.M.R. work.

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THE FALLACY OF THE FRACTURED CLAVICLE

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SOME surgeons believe that a little movement at a fracture site promotes union, and in support they point to the behaviour of the fractured clavicle. The usual argument is that orthodox treatment certainly does not produce fixation, yet union is known to proceed quickly—the suggestion being that the quick union is due to the movement. There are reasons to believe, however, that this is precisely the opposite of the truth, and it seemed desirable to scrutinise the validity of the clavicle argument very carefully.

PROGRESS OF FRACTURED CLAVICLES

Case	Occupation	Time to radiological union (weeks)	Time of return to work (weeks)	Symptoms
1	Messenger	Over 5; less than 9	6	Minor symptoms until 3rd week
2	Grinder	Over 14; less than 48	4	Discomfort when lying on shoulder until 40th week
3	Engineer	Over 16; considerably less than 48	?	Occasional slight pain until after 16th week
4	Butcher	Over 20	3	No symptoms
5	Fitter's mate	Over 13; less than 35	3 (light work)	Slight pain on full movement until 7th week
6	Labourer (painter)	Not much less than 26	2	Some tenderness until 4th week
7	Student	A little less than 11	—	Difficulty with throwing until after 7th week
8	Jeweller	Over 10; less than 13	12	Refracture from minor trauma at 8th week. Symptoms until 11th week. 2nd refracture at 9 months
9	Chef	Over 8; not consolidated at 26	5	Painful to lie on until 8th week and on heavy lifting until 14th week
10	Supervisor	About 10	?	Minor symptoms until 9th week
11	Professional footballer	Not united at 18	9	Painful to lie on until 25th week

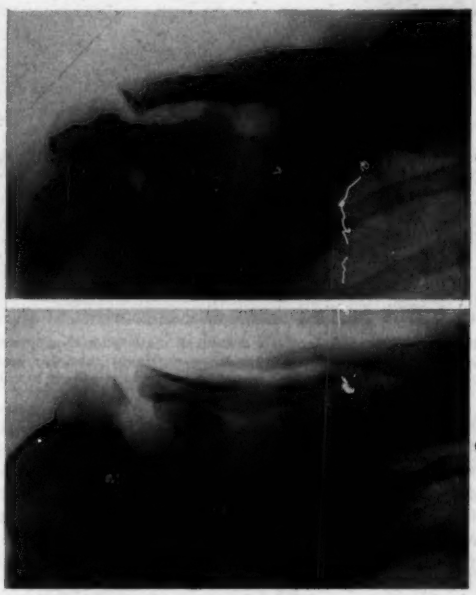

Fig. 1—The possibility of misleading information from a single X-ray view (case 2, fourteen weeks). (*a*) an inferoposterior-superoanterior view in which it is impossible to see whether or not the bone is united; (*b*) a superoposterior-inferoanterior view in which the incomplete union is obvious.

A weakness lies in the fact that no-one seems to have investigated the correctness of either premise—i.e., whether or not the fracture moves during treatment, and whether or not it really does unite quickly. Bohler (1935) is not explicit about speed of union, but is content to remove splintage at three to five weeks. Watson-Jones (1955) says that " . . . the fracture almost invariably unites in about three weeks " but offers no evidence for this statement.

Accordingly the time-to-union in a series of fractured clavicles was assessed radiologically. This series consisted of consecutive cases in adults, and was unselected except for the exclusion of 4 patients who received unorthodox treatment—usually because of some concomitant injury—and of 2 not fully followed-up. Treatment was by the standard figure-of-eight bandage for three or four weeks.

A technique had first to be devised for obtaining two X-ray views, because the conventional single view is liable to give incomplete information (fig. 1). The patient stood obliquely facing a vertical cassette; one view was taken obliquely downwards and one obliquely upwards. A similar technique was described by Quesada in 1926.

Results

The table shows that times-to-union considerably exceed those usually accepted, and that in fact the clavicle as ordinarily treated does *not* unite quickly.

The average was certainly over thirteen weeks. (This figure is an underestimate, since it was obtained by averaging the latest times when the bone was known to be *not* united.) Examples of the true behaviour of this fracture are shown in figs. 1 and 2. Quick union is not completely unknown, but examples are uncommon enough to have escaped this short series. The general conclusion is that quick union is the exception rather than the rule and that the clavicle, therefore, does not behave differently from other bones.

Discussion

The origin of the mistaken impression that union is quick becomes evident when other aspects of the case-

Fig. 2—Absence of union in a fractured clavicle at twenty weeks (case 4). Subsequent changes leave no doubt that this rather poor radiograph really does represent only an early stage in union.

histories are considered (see table). The ununited clavicle seems almost symptom-free. Ordinary activities are resumed well before the bone is united; and in this it resembles the middle metatarsals. Most of the patients in this series had been able to do their jobs for many weeks before the fractures finally united. Case 4, a butcher, whose radiograph is shown in fig. 2, was using a cleaver at five weeks and was bowling at cricket at seven weeks. Thus, anyone judging from the clinical signs and not making use of radiography to check his conclusions would form the opinion that the fractures united early. Most patients did experience minor symptoms for many weeks, the commonest being discomfort or pain when lying on the affected side. Their disappearance coincided with consolidation as seen by X-ray examinations. Thus the delay in union could often be assessed with some certainty.

It is not my intention to suggest that any revision of present treatment is necessary. From the patient's point of view these methods are satisfactory in that he comes to the surgeon with symptoms and goes away without them—or at least well on the way to losing them. Present treatment, even if ineffective, is at least harmless. Thus there is no practical lesson to learn except, perhaps, not to advise the patient too early a return to vigorous activities (see the unfortunate history of case 8). It would be positively harmful if an enthusiasm for follow-up X-rays led to a spate of bone-graftings.

What is harmful at present is the fact that an inaccurate observation has been made to serve as one of the premises in a fundamental argument about non-union. Movement at a fracture site certainly tends to increase the quantity of callus—and in some of the patients in this series there was much callus—but, as will be shown on another occasion, it is a mistake to assume that much callus is synonymous with good union. The behaviour of the clavicle is now found not to support the old hypothesis that a little movement favours union, and may be evidence against it.

Summary

Fractures of the clavicle do not unite any more quickly than fractures of other bones.

The hypothesis that a little movement favours union therefore loses an important part of its supporting evidence.

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LABORATORY DIFFERENTIATION OF CHRONIC BRONCHIAL DISEASE

AN INVESTIGATION OF 117 CASES

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IT has previously been shown that, in studying the bronchial flora, the results of sputum culture can be interpreted more accurately if attention is paid at the same time to the bacteria in the throat (Brumfitt, Willoughby, and Bromley 1957). Direct bronchial swabbing demonstrated that when bronchial pathogens were present in the sputum but absent from the throat they were almost always present in the bronchi. This finding has now been utilised for a comparison of the bronchial flora in chronic bronchitis, bronchial asthma, and obstructive lesions of the bronchi.

The additional help that may be obtained from the appearance of the specimen (macroscopic or microscopic) has also been assessed, in view of the findings of Elmes et al. (1953) and May (1953) that when there is pus in the sputum bronchial pathogens can often be isolated from the same specimen.

Doubt has been cast on the efficiency of sputum culture. Bergman *et al.* (1955) and Tunevall and Wasserman (1956) often failed to recover organisms from sputum in cases where they had been cultured from bronchial aspirates. As this may be related to the irregular distribution of pathogens in the sample of sputum (May 1952), the method of sampling is important. The methods we used proved very efficient when their results were compared with those of direct bronchial swabbing (Brumfitt et al. 1957). Since, in most cases, the sputum has been sampled by more than one method, the present results permit a comparison of the efficiency of these various methods of sputum culture as regards recovery of bronchial pathogens.

Material and Methods

During two years, sputum and throat swabs were examined from 117 patients admitted for investigation of chronic respiratory disease. These patients have been divided into three clinical groups without reference to laboratory findings. 62 were diagnosed clinically as having bronchial asthma and 37 as having chronic mucopurulent bronchitis (4 with demonstrable bronchiectasis in addition). 18 had obstructive bronchial lesions (most often carcinoma).

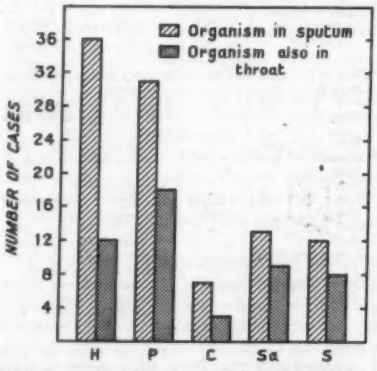

Fig. 1—Incidence of bronchial pathogens in the sputum and throat in 117 cases. H—*Hæmophilus influenzæ*; P—*Pneumococcus*; C—Coliforms; Sa—*Staphylococcus aureus*; S—β-*hæmolytic streptococcus*.

Sputum was examined as described by Brumfitt et al. (1957). Its macroscopic appearance was recorded and graded as purulent, muco-

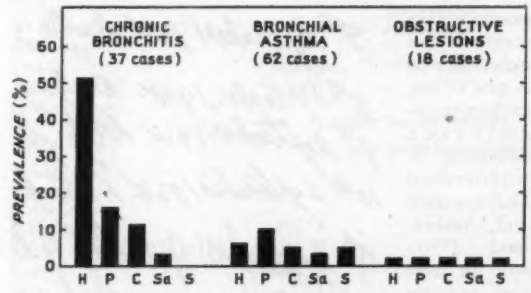

Fig. 2—Incidence of bronchial pathogens in various clinical groups of cases.

purulent, mucoid with traces of purulent material, or entirely mucoid. Giemsa and Papanicolaou stains were applied to smears made from the most opaque portions of the specimen. An approximate assessment of the quantity of pus cells was recorded as +, ++, or +++ depending upon the number of cells found in a representative high-power field. The degree of contamination by throat squames was noted, as was the presence of eosinophils, bronchial epithelial cells, and "dust cells"—viz., histiocytes containing carbon pigment.

Results

In about half of the cases with pathogens in the sputum, the same organisms are also present in the throat (fig. 1). Where the organisms in question are present in the sputum but absent from the throat, they are held to have originated from the bronchi. Using this criterion, one can obtain figures for the relative incidence of various pathogens in the different clinical groups (fig. 2).

The findings in the 37 bronchitis cases have been further analysed to show the incidence of bronchial pathogens singly and in combination:

Hæmophilus influenzæ alone	14
H. influenzæ + pneumococcus	3
H. influenzæ + coliforms	2
Pneumococcus alone	3
Coliforms alone	2
Staphylococcus aureus alone	1
Total	25

In individual cases, the occurrence and numbers of pus cells in stained smears commonly bore no relation to the presence or absence of pathogens on culture; but a higher proportion of smears showing abundant (+++) pus cells came from sputa containing pathogens than from sputa yielding no pathogens (fig. 3). Where the pathogen was thought to have come from the throat rather than from the bronchi, pus cells were rarely abundant.

Again, the presence or absence of visible pus was poorly related, in individual cases, to the occurrence or otherwise

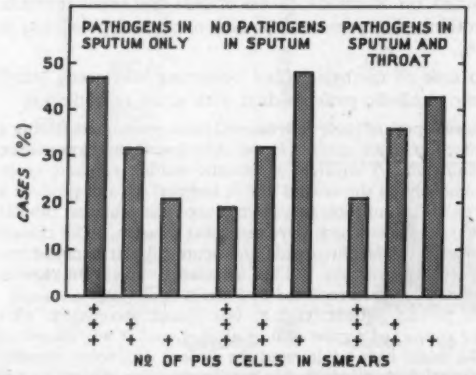

Fig. 3—Assessment of pus cells in sputum related to cultural results.

of pathogens, but there was a tendency for sputa containing pathogens of presumed bronchial origin to be more purulent than those containing no pathogens or pathogens of presumed pharyngeal origin (fig. 4).

In those instances where a number of different methods of sampling sputum were used, it was found that the frequency with which pathogens were isolated varied slightly according to the method used for the cultivation of sputum—51 from mucus only, 57 from pus only, 60 from homogenised sputum, and 62 from combined methods. The same order of efficiency was obtained when the analysis was confined to cases in which the organism in question was believed to be derived from the bronchi.

Discussion

Our results indicate a relatively high incidence in chronic bronchitis of *Hæmophilus influenzæ*, singly or associated with other bronchial pathogens, and a lower incidence of pneumococci, coliforms, and *Staphylococcus aureus*. In half of the cases from which pneumococci and coliforms were isolated, *H. influenzæ* was also present, and may have been the more important pathogen. These findings are similar to those of Mulder (1956). There is no such preponderance of *H. influenzæ* in the patients with bronchial asthma or with obstructive lesions. In all groups the pneumococci would have assumed greater importance if the results of simultaneous throat-swab culture had not indicated that the throat was their probable source. This may partly explain the relatively high incidence of pneumococci reported by Stuart-Harris et al. (1953) and May (1953) in chronic bronchitis.

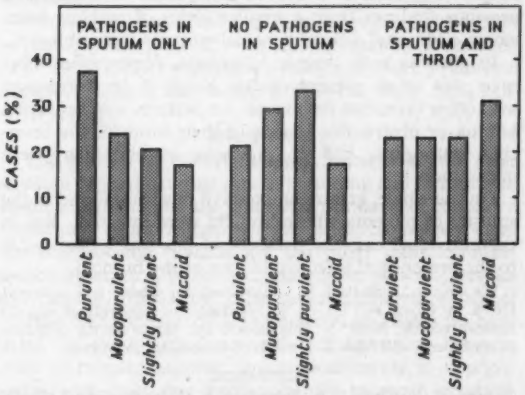

Fig. 4—Macroscopic appearance of sputum related to cultural results

In 12 of the 37 cases of chronic bronchitis, no pathogen could be definitely incriminated. This finding is related to the difficulty of interpretation when an organism is simultaneously found in the throat and sputum (Brumfitt et al. 1957), and also, in part, to the problem of clinical differentiation between chronic bronchitis and asthma.

The presence of pus in the sputum was not always a reliable indication of bronchial infection (figs. 3 and 4); but there was a tendency for pus to be more abundant in patients with pathogens in the sputum only, than in those with either no pathogens, or pathogens in both sputum and throat. This observation adds weight to the contention that the bronchi are less commonly infected in the latter group.

Eosinophils were noted in the sputum of 22 patients. Of these, 19 had asthma and 3 chronic bronchitis. The cultural findings suggested bronchial infection in about a quarter of these cases.

The presence of histiocytes containing carbon pigment (dust cells) or ciliated bronchial epithelial cells in a sample of sputum is good evidence that it is, at least partially, of bronchial origin, and thus increases the significance of the cultural results; while the presence of pharyngeal squames as the predominant cells signifies a heavy degree of throat contamination. No other characteristic cytological criteria of bronchial infection have been noted.

Since several methods of sampling have been used, it is of interest to compare their relative efficiency. Homogenisation of whole sputum appears most efficient, while sampling of the purulent portions is only slightly less so. Sampling a non-purulent portion was the least efficient. These results partially reconcile the views of May (1953), who advocates enzymatic digestion, and Allibone et al. (1956), who recommend a large sample of pus for the culture of pathogens from sputum.

Summary

117 patients with chronic bronchial disease have been investigated by culture of simultaneous sputum and throat swabs. The results have been interpreted in the light of previous findings from a smaller series of patients from whom additional direct bronchial cultures were obtained.

In patients with chronic bronchitis, *Hæmophilus influenzæ* was often present, either alone or in association with other bronchial pathogens. In patients with bronchial asthma or obstructive lesions of their bronchi, the bronchial pathogens, and *H. influenzæ* in particular, were uncommon.

On the whole, greater amounts of pus were found in the sputum of patients whose bronchi were infected. But in the individual case the presence of pus was a poor guide to the presence of infective lesions of the bronchi.

We wish to thank Prof. R. Cruickshank for advice and criticism, Dr. A. A. Glynn and Dr. A. W. Frankland for supplying us with the clinical records, Sister N. Wiggin and her nurses for the collection of specimens, and Miss S. Dodman for technical assistance.

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ACUTE RENAL FAILURE DUE TO POISONS AND DRUGS

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WE have already reported our clinical experience of acute renal failure due to concealed accidental hæmorrhage of pregnancy, criminal abortion, and intravascular hæmolysis (Bull et al. 1955, 1956, 1957), and we now record our cases of acute renal failure due to poisons and drugs.

Poisons

Accidental and suicidal poisonings leading to acute renal failure are uncommon in this country. Thus, for example, in contrast with experience in America, carbon-tetrachloride poisoning is uncommon (Kirkpatrick and Sutherland 1956), and we have not encountered a case. Mercury poisoning is also rare, and we have seen only 3 cases (cases 1–3), of which 2 were due to suicidal attempts and 1 was accidental. Renal failure was moderately severe, and anuria lasted eight days in 1 case and eleven days in the 2 others. None received dimercaprol within the effective period of the first hour of mercury absorption. Vomiting, diarrhœa, and stomatitis were all troublesome features, and 1 patient had a disturbance of the central nervous system (usually recognised only in industrial mercury poisoning) in the diuretic phase (fig. 1).

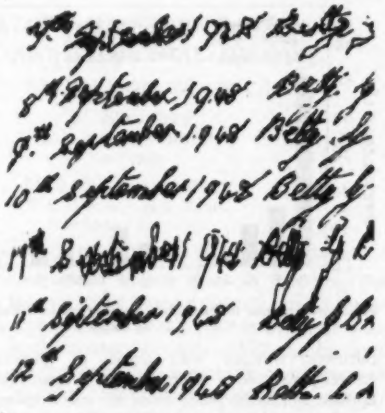

Fig. 1—Case 2: serial specimens of handwriting in early diuretic phase of acute tubular necrosis due to suicidal poisoning with mercury.

1 case of suicidal oxalic-acid poisoning (see appendix, case 4) was seen. Renal failure was severe, and the patient died on the twenty-second day of illness without having achieved a satisfactory diuresis. Conservative management, including hypertonic glucose infusion into the inferior vena cava and retention enemata of ion-exchange resin in the sodium cycle, was applied carefully; the patient might possibly have been kept alive longer if dialysis methods had been available. Poisoning with hydrochloric acid was rapidly fatal in 1 case (case 5) due chiefly to acid erosion in the respiratory and upper alimentary tracts, and acute tubular necrosis was an incidental finding. We have encountered several cases of attempted suicidal phenol poisoning and 1 case of accidental turpentine poisoning, but all the patients recovered, and none had anuria. The patient with turpentine poisoning had urine that smelled of violets and contained numerous red blood-cells initially. In the patients with phenol poisoning the urine was usually concentrated and contained, on occasions, excess of cells and small amounts of protein. A representative case of phenol poisoning is case 6.

No case of methyl-alcohol poisoning was seen, but 2 chronic alcoholic patients died with acute renal failure:

The first patient (case 7) developed lobar pneumonia during a prolonged drinking spree. He was dehydrated and hypotensive on admission. Two litres of isotonic sodium sulphate given intravenously on the second day in hospital did not produce a diuresis. This infusion may have caused the proximal tubular hydropic changes which were seen post mortem. The clinical diagnosis of lobar pneumonia and acute tubular necrosis was confirmed at necropsy. This association in severe chronic alcoholism has been reported by Parrish et al. (1955).

The second patient (case 8) was found unconscious after having consumed a great deal of alcohol, and it was suspected that he might have adulterated the alcohol with some preparation from his chemist's shop. Renal cortical necrosis is known

to develop after immoderate consumption of alcohol and can also be caused by numerous chemical poisons (Sheehan and Moore 1952). Cortical necrosis was suspected clinically in this patient and confirmed post mortem.

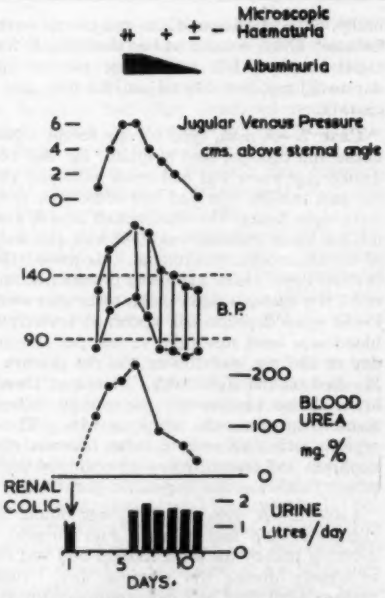

Fig. 2—Case 9: rise in blood-pressure and venous pressure probably due to overloading with water and salt during anuria due to sulphonamide obstruction. On the 13th day the effective renal plasma flow (p-aminohippurate clearance) was 601 ml. per min. and the glomerular filtration-rate (thiosulphate clearance) 93 ml. per min.

Drugs

Our only experience of acute renal failure after drug administration has been with the sulphonamide group. These are known to give rise to renal failure from obstruction by crystalline deposits and epithelial debris in the urinary pathways and from hypersensitivity lesions in the kidneys, particularly acute tubular necrosis and renal arteritis.

Sulphonamide Obstructive Anuria

We have seen a good many cases of sulphonamide crystalluria with hæmaturia and renal colic. Only 5 patients, however, had anuria of any note (cases 9–13 and fig. 2). 1 patient developed cystitis following urethral catheterisation and, when cystoscopy was done, the ureteric orifices could not be located and the cystoscope was pushed through the friable bladder wall. The patient was moribund from peritonitis when we saw him. The 4 other patients appeared to have spontaneous diureses. When diuresis appeared to start after unsuccessful attempts at ureteric catheterisation, it was our impression that this was due to the moving about of the patient on the journey to the theatre. Kolff (1955) emphasises that a rough trip in an ambulance is a good therapeutic measure for such patients. Our present policy is to treat conservatively and to avoid urological manipulations. Hopper and Partridge (1950) point out that in 82 out of 84 collected cases of sulphonamide obstructive anuria the patients recovered. The average onset of diuresis was at 3·1 days and the range was from one to eleven days.

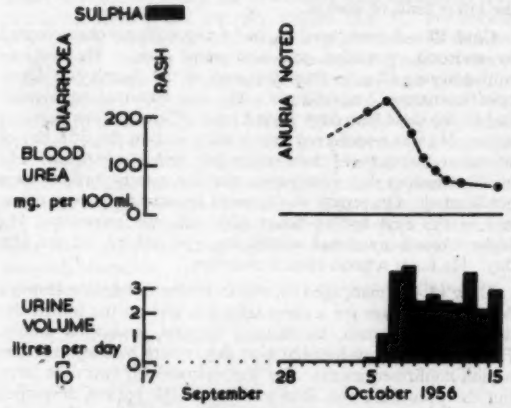

Fig. 3—Case 16: anuria associated with dermatitis and presumably due to sulphonamide sensitivity.

Sulphonamide-sensitivity Anuria

3 patients developed acute renal failure apparently as a sensitivity reaction to sulphonamide drugs (cases 14–16 and fig. 3). They all had associated dermatitis, and in 1 case this started after exposure to the sun. The renal failure was more severe, and the anuria of longer duration, than in sulphonamide obstructive anuria. 2 patients recovered on conservative management. The 3rd patient died partly from rather poor management of the anuria and partly from pyelonephritis superimposed on the tubular necrosis and possibly due to ureteric catheterisation.

Renal failure due to potentially hæmolytic drugs—e.g., quinine and mephenesin—has been discussed in a previous paper on anuria following intravascular hæmolysis (Bull et al. 1957).

Anuria has been noted to follow exposure of the kidney to radio-opaque material—e.g., in aortography (Dormandy et al. 1957) and in retrograde pyelography with pyelorenal backflow (Grieve and Lowe 1955)—but these complications are rare.

Discussion

The pattern of disturbed renal function in our cases of acute tubular necrosis due to poisoning and to sulphonamide sensitivity was the same as in our cases of concealed accidental hæmorrhage, intravascular hæmolysis, and criminal abortion, which are the other most common causes of acute tubular necrosis in our series. Despite the varying histological pictures and different types of tubular damage described by Oliver et al. (1951) we have failed to show any functional differentiation between cases of tubular necrosis due predominantly to nephrotoxins and cases due predominantly to renal ischæmia (Bull et al. 1950, Lowe et al. 1954, Emslie-Smith et al. 1956). As regards sulphonamide obstructive anuria we have studied renal function in only 1 case (case 9), in which there was a much earlier recovery of function than would be expected in tubular necrosis (fig. 2).

Acute renal failure due to poisonings and sulphonamide (either obstruction or sensitivity) should carry a high recovery-rate with adequate treatment. The 2 deaths among our sulphonamide cases were probably avoidable. In mercury poisoning there is very extensive tubular necrosis (Allen 1951), but its reversibility is shown by the excellent recovery made by our 3 patients. The death due to hydrochloric-acid poisoning was due to associated damage of the respiratory and alimentary tracts, renal failure being incidental, and the death due to oxalic-acid poisoning was unexplained and took place when the patient was in the recovery phase of the renal lesion. Our cases of phenol poisoning have been mild, and we have not encountered a fatal case.

Summary

Of 5 cases of acute tubular necrosis due to poisons 3 were due to mercury and 1 each to oxalic and hydrochloric acids. The patients with mercurial tubular necrosis recovered, but the 2 others died. Only very mild cases of phenol and turpentine poisoning were encountered, and none of the patients had anuria. 2 chronic alcoholics died in renal failure after drinking bouts: one had lobar pneumonia and acute tubular necrosis; the other had renal

cortical necrosis. There were 5 cases of sulphonamide obstructive anuria and 3 of sulphonamide sensitivity with renal failure; 1 patient in each group died.

Appendix

Case 1.—A woman, aged 36, was prescribed mercuric-chloride tablets for use in vaginal douching for vaginitis. She used too concentrated a solution and developed a severe vaginal irritation with vomiting, diarrhœa, and a brisk diuresis that was followed within a few hours by anuria. Dimercaprol was not given until the fourth day of anuria. She was treated by the intragastric regime (Bull et al. 1949) and with the artificial kidney on the tenth day of anuria. Her blood-urea level rose to a maximum of 325 mg. per 100 ml., and diuresis developed on the twelfth day. She made a good clinical recovery.

Case 2.—A woman, aged 21, swallowed some mercuric oxide in a suicidal attempt. Faintness, vomiting, and anuria followed. She was treated with gastric lavage but had no dimercaprol. Anuria persisted for eleven days, and her maximal blood-urea level was 380 mg. per 100 ml. She was treated conservatively by the intragastric regime and made a good clinical recovery. Convalescence was delayed by disturbance of her central nervous system in the early and late diuretic phases. The chief features were tremor, ataxia, and dysarthria of the type seen in industrial mercury poisoning. Her incoordination is evident from her handwriting (fig. 1).

Case 3.—A woman, aged 23, swallowed some " hair-curling tonic " (which contained mercuric chloride 24 g. per packet). She collapsed with immediate abdominal pain and was taken to hospital, where her stomach was washed out. She had bloody diarrhœa, vomiting, and anuria. Dimercaprol was not given until the second day. With careful conservative management she made a good recovery after eight days' anuria.

Case 4.—A woman, aged 30, was admitted to hospital some hours after swallowing a teaspoonful of oxalic-acid crystals. Her stomach was washed out, and she had an intravenous infusion of noradrenaline in physiological saline solution for shock. She had anuria and then severe oliguria, and her blood-urea level rose to 450 mg. per 100 ml. on the sixteenth day. Thereafter she entered the early diuretic phase, and her blood-urea level began to fall. Treatment was by intravenous infusion of hypertonic glucose into the inferior vena cava and with retention enemata of sodium-charged cation-exchange resin. Unfortunately she had an unexplained profound circulatory collapse on the twenty-second day and died. Necropsy confirmed the diagnosis of acute tubular necrosis.

Case 5.—A man, aged 54, was admitted to hospital some hours after swallowing an unknown quantity of hydrochloric acid in a suicidal attempt. On admission emergency tracheotomy was done for laryngeal obstruction due to œdema. He was very restless and had gross excoriation in the mouth and generalised râles in the lungs. His blood-pressure was 120/90 mm. Hg. Since he did not pass urine that day he was catheterised at night; 300 ml. of dark brown urine was obtained, and its specific gravity was 1·020. Only small quantities were obtained by catheter from that time until death forty-eight hours later, the total amounting to 200 ml. The urine was dark, of specific gravity 1·010, and contained pigmented casts. The blood-pressure remained between 110/70 and 140/90 mm. Hg until shortly before death. At necropsy there were gross signs of acid erosion in the air passages and upper gastro-intestinal tract, pulmonary œdema, and bronchopneumonia. Histologically the kidneys showed acute tubular necrosis, with a few pigment casts in the collecting tubules.

Case 6.—A woman, aged 61, drank half a cupful of ' Lysol ' in a suicidal attempt. She was found unconscious and was brought into hospital, where she recovered consciousness rapidly. Her general condition was good, her blood-pressure was 145/70 mm. Hg, and there were brownish staining on her chin and ulceration in her mouth. The first samples of urine showed carboluria and were well concentrated (urinary urea 1800–3200 mg. per 100 ml.). Treatment consisted of olive oil orally, prophylactic penicillin, and careful water and electrolyte balance. Urine volume was on the low side for a few days; the blood-urea level fell from 60 mg. per 100 ml. on the second day to 20 mg. per 100 ml. on the fifth day. She recovered quickly.

Case 7.—A man, aged 42, was found semiconscious in his house and brought into hospital. He had been a very heavy drinker for years and had been indulging excessively during the past month. He had had some pain in his left chest for forty-eight hours. On examination he was drowsy and breathless, his blood-pressure was 80/50 mm. Hg, and there were signs of left lower lobar pneumonia. He passed 180 ml. of urine on the first day. There was heavy proteinuria, and many red cells and a few granular and cellular casts were seen microscopically in the spun deposit. He remained severely oliguric, and his blood-urea level rose from 96 mg. per 100 ml. on the second day to 496 mg. per 100 ml. on the seventh day in hospital. He died on the eighth day. Necropsy showed resolving left lower lobar pneumonia, pulmonary œdema, and several hæmorrhages into the trunk muscles. The kidneys showed typical lesions of acute tubular necrosis affecting the distal nephrons and severe hydropic swelling of the proximal tubular cells. There was also very mild glomerulitis.

Case 8.—A man, aged 27, was found unconscious in a chemist's shop and brought into hospital. He had been drinking heavily for some months and had consumed a bottle of whisky during the previous day. Examination of the cerebrospinal fluid and radiography of the skull were normal. He recovered consciousness but was hallucinated and required sedation with paraldehyde. Despite good general condition and a blood-pressure of 124/64 mm. Hg he had very severe oliguria, with red cells and hyaline and granular casts in his urine. He developed epileptiform fits, and his blood-urea level rose to 155 mg. per 100 ml. on the third hospital day, when he died. Necropsy confirmed the clinical diagnosis of renal cortical necrosis.

Case 9.—A man, aged 34, had 30 g. of sulphadiazine during outpatient treatment of gonorrhœa. He developed renal colic, hæmaturia, and then anuria. Two attempts at ureteric catheterisation, one under spinal anæsthesia, failed, and after two days' anuria he was transferred to our care. He had been grossly overloaded with salt and water and had developed hypertension, increased jugular venous pressure, basal crepitations in the lungs, and œdema. On the fourth day he was cystoscoped under local anæsthesia. His bladder mucosa was injected and œdematous. A ureteric catheter was passed a few centimetres up the left ureter, and some epithelial debris was removed. No crystals were seen microscopically. In the next twelve hours he passed 275 ml. urine and subsequently he made a good clinical recovery. Data are shown in fig. 2. Note that renal function tests on the thirteenth day were near the lower limit of normal.

Case 10.—A man, aged 25, had a vague illness characterised by anorexia, vomiting, and abdominal pain. He received sulphadiazine 20 g. in four days and on the fourth day developed hæmaturia and oliguria. He was admitted to hospital and in the next four days passed only 275 ml. of bloodstained urine. He was transferred to our care, and on the fifth day of anuria cystoscopy was done under low spinal anæsthesia. His bladder mucosa was œdematous, and the ureteric orifices were not located. On return to the ward he started to pass urine, and in the next twelve hours 4200 ml. was recovered. His highest blood-urea level was 93 mg. per 100 ml. on the fifth day. He made a good clinical recovery.

Case 11.—A man, aged 63, was treated with sulphamezathine 24 g. in four days for a chest infection and on the fourth day developed loin pain, hæmaturia, oliguria, and then anuria. He was admitted to hospital next day, where bladder catheterisation confirmed anuria. He was cystoscoped two days later, but the procedure was abandoned after the patient developed severe shock. The cystoscope had perforated the œdematous inflamed bladder wall, but this fact was not appreciated at the

time. Paralytic ileus developed, and he was transferred to our care. He died on the sixth day of anuria. Necropsy showed peritonitis due to traumatic perforation of the bladder wall.

Case 12.—A man, aged 45, was treated with sulphamezathine 12 g. for tonsillitis and then developed renal colic, hæmaturia, and then anuria. An attempt at ureteric catheterisation failed on the fifth day, and he was transferred to our care. Spontaneous diuresis developed on the sixth day, however, and he made a good clinical recovery. His highest blood-urea level was 130 mg. per 100 ml. on the fifth day.

Case 13.—A woman, aged 42, was treated for a chest infection with sulphamezathine 19 g. in three days. She then developed renal colic, hæmaturia, and anuria. She remained anuric for three days and then had a rather gradual diuresis. Her highest blood-urea level was 106 mg. per 100 ml. on the fifth day.

Case 14.—A woman, aged 54, was treated with 12 g. of a sulphonamide drug (the exact preparation was unknown) for an upper respiratory infection. She developed a skin rash and oliguria, and the drug was stopped. She was admitted to hospital three days later and was treated with alkalis and intravenous fluids. Ureteric catheters were passed and the renal pelves washed out with bicarbonate solution. There was no evidence of ureteric obstruction, and no crystalluria was evident. On the eighth day of anuria she was transferred to our care. She was drowsy and œdematous and had bronchopneumonia and severe dermatitis. She died on the tenth day. Necropsy showed staphylococcal bronchopneumonia, acute tubular necrosis, pyelonephritis, and multiple abscesses in the left kidney. Tubular necrosis was considered to be due to sulphonamide sensitivity, and the pyelonephritis and renal abscesses were thought to be superimposed lesions due to infection following ureteric catheterisation.

Case 15.—A man, aged 65, was treated with phthalylsulphathiazole preoperatively for rectal carcinoma. Dermatitis and oliguria developed. Cystoscopy was performed ; only the right ureter could be catheterised, and no abnormality was found. The blood-urea level, which had been 25 mg. per 100 ml. on admission, rose to 254 mg. per 100 ml., and then with spontaneous diuresis, fell to 74 mg. per 100 ml. At this time the patient's general condition was fair, and he had an exacerbation of chest infection. Palliative colostomy was done after preparation with blood-transfusion and breathing exercises.

Case 16.—A woman, aged 62, developed diarrhœa, and after eight days she consulted her doctor, who prescribed sulphaguanidine. Next day severe dermatitis began while she was sitting in the sunlight. The rash spread, and the drug was stopped after three days. Two days later left basal pneumonia developed, and was treated with erythromycin. On the twelfth day after starting drug therapy she had anuria, and on the sixth day of anuria she was admitted to hospital. Diuresis began two days later, and her blood-urea level fell rapidly from its highest level of 230 mg. per 100 ml. (fig. 3). No crystals were present in freshly voided urine at the onset of diuresis. In the early diuretic phase there were poor concentration of urine and failure of conservation of sodium and potassium. On the twelfth day after onset of diuresis a water load of 1 litre led to a maximal flow of 9 ml. of urine a minute, which was reduced to 1 ml. a minute after the intramuscular injection of 5 units of posterior pituitary extract, thereby showing the return of tubular function. Patch-testing during convalescence confirmed sulphonamide sensitivity. The patient's daughter, like her mother, developed an acute skin eruption after treatment with sulphonamide ; neither had been treated before with sulphonamide.

We are grateful to Dr. Robert Semple for permission to include case 8.

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AN ATYPICAL CARCINOID TUMOUR SECRETING 5-HYDROXYTRYPTOPHAN

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THE syndrome associated with metastasising argentaffinoma has now been well documented, and it seems likely that many of the manifestations are due to an excess of 5-hydroxytryptamine elaborated by the tumour. Among the many cases published, a few, including the third patient described by Snow et al. (1955), present certain atypical features. Prompted by the similarity to another atypical patient described by Smith et al. (1957), we have reinvestigated this patient. Our findings suggest that he may belong to a distinct clinical group in which the tumours produce 5-hydroxytryptophan instead of 5-hydroxytryptamine.

Case-report

A detailed clinical description of this man, aged 45, has already been published (Snow et al. 1955). To summarise, flushing attacks precipitated by food and particularly by alcohol had been present for more than twenty years. The flush was patchy and bright red, and could be attenuated by anti-histamine therapy. Diarrhœa had never been a feature. The patient was first observed four years ago, when his hard enlarged palpable liver was found at laparotomy to be full of metastases from a small primary tumour in his stomach. The hepatic enlargement has remained unchanged up to now, and there has been no deterioration in his general condition, which remains excellent. His main complaint continues to be of intermittent attacks of pain caused by a duodenal ulcer, whose presence was confirmed at the laparotomy. Additional radiological investigations since the previous report on this patient have included intravenous pyelography and a skeletal survey, neither of which has revealed any abnormality.

Further Investigations

Methods

Urinary 5-hydroxytryptamine was estimated in our respective laboratories either by the colorimetric method of Udenfriend et al. (1955b) or by the same 1-nitroso-2-naphthol colour reaction after adsorption on a column of 'Amberlite IRC 50' and elution with sulphuric acid, a standard being carried through the whole procedure. The results obtained by the two methods were in close agreement. Urinary 5-hydroxyindoleacetic acid was estimated by the method of Udenfriend et al. (1955a) or by the method of Macfarlane et al. (1956), both of which gave comparable results. "Total 5-hydroxyindoles" were measured as the colour reaction produced by 1-nitroso-2-naphthol with the unextracted urine with 5-hydroxyindoleacetic-acid standards. Chromatography of the

DR. BULL AND OTHERS: REFERENCES—*continued*

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TABLE I—PARTITION OF 5-HYDROXYINDOLES IN URINE FROM BLADDER

Specimen no.	1		2		3
—	mg. per g. of creatinine	mg. per 24 hr.	mg. per g. of creatinine	mg. per 24 hr.	mg. per g. of creatinine
"Total 5-hydroxyindoles"	110	110	99·4	117·0	98
5-Hydroxytryptamine	18	18	20·4	24·0	20
5-Hydroxyindoleacetic acid ..	43	43	50·3	59·4	47
Balance = 5-hydroxytryptophan ..	49	49	28·7	33·6	31

urine for indoles was kindly carried out by Dr. C. E. Dalgliesh (Dalgliesh 1955, 1956). Indole chromatography was also done by the method of Jepson (1955) on ultrafiltered desalted serum and on urine. The presence of 5-hydroxytryptamine on chromatograms was confirmed by the method of Jepson and Stevens (1953).

This histamine content of the urine was kindly estimated by Dr. R. S. Stacey, using the method described by Roberts and Adam (1950).

Chromatography

Chromatographic examination was carried out on bladder urine and on separate specimens obtained from each ureter. 5-Hydroxytryptophan was present in all the specimens, and 5-hydroxytryptamine, 5-hydroxyindoleacetic acid, and unknown slow-running Ehrlich-reacting spots, presumed to be conjugates, were also found in bladder urine. There were insufficient 5-hydroxyindoles in the serum to show on the chromatogram. Indole chromatograms were also prepared from the urine of six healthy people who had been given DL-5-hydroxytryptophan intravenously during another investigation (Pare and Sandler, to be published). Apart from an absence of conjugates, these were strikingly similar to those obtained from our patient's urine.

Quantitative excretion of 5-hydroxyindoles.—Bladder specimens of urine recently obtained and submitted to quantitative partition of 5-hydroxyindoles gave the results shown in table I. The 5-hydroxyindoleacetic acid excreted by this patient has been determined on numerous occasions and is fairly constant at 40–50 mg. per g. of creatinine or 40–60 mg. per twenty-four hours. The amount of 5-hydroxytryptamine excreted has been determined chemically on several occasions and agrees fairly closely with that originally determined pharmacologically (Snow et al. 1955). If the sum of 5-hydroxytryptamine and 5-hydroxyindoleacetic acid is subtracted from the " total 5-hydroxyindoles ", the result is a function of the level of 5-hydroxytryptophan (Udenfriend et al. 1957) and can be used as such for comparing different specimens.

Ureteric specimens of urine from right and left ureters are compared in table II as regards partition of 5-hydroxyindoles.

TABLE II—PARTITION OF 5-HYDROXYINDOLES IN URINE FROM URETERS

—	mg. per g. of creatinine	
	Lt ureter	Rt ureter
" Total 5-hydroxyindoles "	80·0	81·0
5-hydroxytryptamine	13·0	10·8
5-hydroxyindoleacetic acid	7·8	12·4
Balance = 5-hydroxytryptophan	59·2	57·8

Excretion of Histamine

From examination of an isolated specimen histamine excretion had previously been stated to be within normal limits (Snow et al. 1955), but further estimations have repeatedly revealed a high output, 480–940 μg. per twenty-four hours, the normal range being 18–62 μg. (Roberts and Adam 1950).

Discussion

Enough cases of argentaffinoma syndrome have now been published for a fairly constant clinical picture to emerge which, broadly, varies directly in severity with the mass of tumour present. It has been presumed, from the high level of 5-hydroxytryptamine found in the tumour, that this substance is liberated into the blood-stream. Certainly the urinary 5-hydroxyindole pattern produced after the experimental injection of 5-hydroxytryptamine (Erspamer 1956) resembles that found in the argentaffinoma syndrome—i.e., a large excess of the metabolite 5-hydroxyindoleacetic acid with only a small increase in 5-hydroxytryptamine.

When our patient was first described (Snow et al. 1955), a large urinary excretion of 5-hydroxytryptamine and a comparatively small one of 5-hydroxyindoleacetic acid were noted, together with other anomalies, for which at that time there was no obvious explanation. Recently, however, Smith et al. (1957), found in a patient with the carcinoid syndrome a large urinary excretion of 5-hydroxytryptamine and of 5-hydroxytryptophan, its precursor. This aminoacid, derived from dietary tryptophan, had not previously been found in other than trace amounts, and it was postulated that renal metastases were secreting intermediary metabolites direct into the urine. The intravenous pyelogram was considered to support this view, but Dick et al. (1957), in a further report on the same patient, state that retrograde pyelography showed no abnormality.

Since our patient also had a large urinary output of 5-hydroxytryptamine, urinary chromatography was carried out, whereupon large amounts of 5-hydroxytryptophan were found as well as 5-hydroxytryptamine and 5-hydroxyindoleacetic acid. Intravenous pyelography did not reveal any obvious renal metastases in our patient, however; so ureteric catheterisation was done in an attempt to locate the fault, urine being collected from each ureter separately. Indole partitioning gave similar results in both specimens; and, unless bilateral metastases of equal mass were present, which was unlikely, the explanation advanced by Smith et al. (1957) cannot apply to our patient.

Although Dick et al. (1957) estimated the 5-hydroxyindoleacetic acid in ureteric specimens from their patient they took no account of possible differences in urine flow by relating the level of 5-hydroxyindoleacetic acid to that of creatinine. The difference they found between the two specimens may therefore not be significant.

Chromatograms of our patient's urine bore a striking resemblance to those obtained from urine passed after intravenous injection of 5-hydroxytryptophan into six normal subjects. It therefore seemed likely that the principal metabolite of the tumour was 5-hydroxytryptophan, which, when released into the blood-stream, was decarboxylated to 5-hydroxytryptamine elsewhere. 5-hydroxytryptophan-decarboxylase activity is known to be widespread (Gaddum and Giarman 1956); and since the level of 5-hydroxytryptophan decarboxylase is especially high in the kidneys (Clark et al. 1954), the large output of 5-hydroxytryptamine could be due to direct decarboxylation there. 5-Hydroxytryptophan which reached the kidney and escaped decarboxylation would pass unchanged into the urine, and the other major indole fraction, 5-hydroxyindoleacetic acid, would arise from 5-hydroxytryptophan decarboxylated at extrarenal sites and further

TABLE III—RELEVANT CLINICAL AND BIOCHEMICAL FEATURES OF THREE ATYPICAL CASES COMPARED AND CONTRASTED WITH "TYPICAL ARGENTAFFINOMA"

—	Present case	Case of Smith et al. (1957)	Case of Waldenström et al. (1956)	Typical argentaffinoma
Histology	Atypical, no argentaffin granules	Atypical, no argentaffin granules	Atypical, no argentaffin granules	Characteristic argentaffin granules
Distribution of metastases	Mainly hepatic	Hepatic and osseous	Hepatic and osseous	Hepatic
Type of flushes	Bright-red "histamine type"	Not discussed in detail	Bright-red "histamine type"	Mixed cyanosis, erythema, and pallor
Excretion of histamine	Great increase	Great increase	Great increase	Slight increase
Urinary 5-hydroxytryptophan (chromatographic)	Present	Present	Not stated	Absent
Urinary 5-hydroxytryptamine	Great increase	Great increase	Great increase	Slight increase
5-Hydroxytryptamine in tumour	Small amounts	High level	Not stated	High level

metabolised by monoamine oxidase. The presence of relatively greater amounts of 5-hydroxytryptophan in the ureteric specimens is compatible with a sudden release of large quantities of it in response to an agent used for inducing or for maintaining general anæsthesia, during which striking and prolonged flushing was noted.

It was originally reported that, although tumour tissue from our patient undoubtedly resembled that of a carcinoid tumour, no typical argentaffin granules were found (Prof. A. C. P. Campbell). Jacobson (1954) has emphasised the distinction, based on differential staining, between granular argentaffin cells (found in typical argentaffinomata) and argyrophil cells, which have no granules. Dr. Jacobson kindly examined material from our patient and reported that all the cells were argyrophil. This finding fits in well with the site of the primary tumour in the stomach, where argyrophil cells are numerous but argentaffin cells less common.

It is obviously tempting to suggest that argyrophil cells may form 5-hydroxytryptophan, whereas argentaffin cells, tumours of which are known to contain 5-hydroxytryptophan decarboxylase (Langemann 1956, Giarman et al. 1957), form 5-hydroxytryptamine, but investigation of such a hypothesis will have to await the availability of more tumour tissue. There is no inherent improbability, however, in the idea that each type of cell may have a different function, and that tumours may contain different proportions of each. A precedent for a tumour with two distinct secretions has already been established in the phæochromocytoma, which may produce different amounts of noradrenaline and adrenaline. This hypothesis may explain the high levels of 5-hydroxytryptamine in tumour tissue of the otherwise similar patient of Smith et al. (1957), compared with the very low level of 5-hydroxytryptamine in tumour tissue of our patient.

Another patient, having features in common with both our own and Smith's patient, was described by Waldenström et al. (1956). Although the urinary indole chromatographic pattern was not described, higher levels of urinary 5-hydroxytryptamine were obtained by pharmacological assay than in any of the large number of patients with argentaffinoma investigated by these workers (Pernow and Waldenström 1957). Other atypical features suggesting the possible clinical identity of these three patients are shown in table III.

Neither Smith et al. (1957) nor Dick et al. (1957) give a detailed clinical description of the flushing attacks in their patient, but the atypical bright-red persistent flush of "geographical" pattern reported by Waldenström et al. (1956) and also seen in our patient, which could be attenuated by anti-histamine therapy, correlates well with the enormous output of urinary histamine in all three patients. 5-Hydroxytryptamine is a mild histamine liberator (Feldberg and Smith 1953); so it is not surprising that several patients with the typical argentaffinoma syndrome had an increased output of histamine (Pernow and Waldenström 1957), but usually the levels attained are lower than those found in the three patients under discussion.

It is improbable that the tumour produces histamine, and Waldenström et al. (1956) did not detect any in biopsy material from their patient. We found no direct histamine-releasing action of 5-hydroxytryptophan on intradermal injection in normal subjects (unpublished observation), but widespread peripheral production of 5-hydroxytryptamine resulting from the excess 5-hydroxytryptophan may have a more pronounced histamine-releasing effect than have the relatively small amounts of free plasma-5-hydroxytryptamine in the typical syndrome.

We suggest that the anomalous findings in the three patients discussed can best be explained by the existence of a distinct clinical group of tumours producing 5-hydroxytryptophan.

Summary

A patient with the carcinoid syndrome having many atypical features, including urinary excretion of 5-hydroxytryptophan, is described.

It is suggested that this case and two others published, form a new clinical group of tumours which secrete 5-hydroxytryptophan.

We wish to thank Dr. H. T. Howat for permission to investigate this patient; Mr. M. Bell, of the clinical laboratory, Manchester Royal Infirmary, for some of the 5-hydroxyindole estimations; Miss Lilith Emslie for expert technical assistance, and the Royal Free Hospital Endowment Fund for defraying her salary; Dr. D. N. Baron and Dr. D. A. K. Black for helpful criticism; and Prof. K. R. Hill for providing facilities.

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INFLUENZAL ENCEPHALITIS

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ALTHOUGH cases of acute hæmorrhagic encephalitis were described as early as 1892 (Leichtenstern, Furbringer, Koenigsdorf) and were undoubtedly seen in the pandemics of influenza in 1890 and 1918, there have been few reports in recent years.

Leigh (1946) described 2 cases of encephalitis during the influenza type-B epidemic of that year; Holmes (1947) recorded encephalitic symptoms following atypical pneumonia; and Jennings (1952) reported a case in which a patient with basal pneumonia and a rising type-A antibody titre developed neck stiffness and an abnormal cerebrospinal fluid (C.S.F.).

Of 91 cases of encephalitis notified in England in 1951, 4 were listed as postinfluenzal (Conybeare 1952). Crome (1954) reported 3 adult cases of encephalitis occurring in Slough during the 1951 epidemic of influenza type-A. Fernandez (1956) described a fulminating encephalitis in 7 infants, which he thought followed on influenza.

During the current epidemic of influenza type-A (" Asian flu ") 2 children with an encephalitic illness were admitted to Queen Mary's Hospital for Children within three days of each other. Both attend school in Caterham and had had recent contact with influenza at school and at home. The clinical course was so similar that we believe that they had the same disease.

Case-histories

Case 1.—A girl, aged 13, was admitted at 8 A.M. on Oct. 17. After being at home with a severe cold for two weeks she had returned to school on Oct. 15. Her nose was still blocked and she had a slight cough. On the 16th she felt drowsy after coming home from school. She was restless and moaned throughout the night. At 6 A.M. she was found to be unrousable and incontinent of urine.

On admission she was severely ill, unconscious, and very restless and irritable, with some degree of photophobia. There was very little response to painful stimuli. Her neck was slightly stiff and Kernig's sign was positive. The right pupil was smaller than the left but the light reflexes (direct and consensual) were unimpaired. The tone of the limbs was increased, with variable rigidity and athetoid movements of the arms (somewhat reminiscent of cerebral palsy). On the left side the biceps-jerk was absent, the knee-jerk increased, and the plantar response extensor.

There were crepitations in both lung fields but no other pneumonic signs. Temperature 97°F; pulse-rate 120 per min.; respirations 25 per min. and regular. The C.S.F. was clear and colourless, with 6 lymphocytes per c.mm., and protein 50 mg. and sugar 75 mg. per 100 ml. Globulin was not increased, and no organisms were found on staining or subsequent culture. Blood-count: 9000 white cells per c.mm (neutrophils 78%, lymphocytes 17%, monocytes 5%). Blood-sugar and blood-electrolyte levels normal. Urine contained acetone.

She was given prophylactic penicillin, intravenous dextrose-saline solution, and paraldehyde to control the restlessness.

On the evening of admission (Oct. 17) her temperature was 102°F and her condition critical. There was no change in the level of consciousness. Both pupils showed repeated variation in size and in response to light.

On Oct. 18 she was still in coma but swallowed small quantities of fluid. She was still incontinent of urine. In addition, hyperventilation and mild tetany developed. The C.S.F. was again clear, with 10 lymphocytes per c.mm. and protein 35 mg. and sugar 80 mg. per 100 ml. Direct smear and culture again negative.

On Oct. 19 her general condition was better and she seemed to improve for short spells when she would open her eyes and gaze about.

On Oct. 20 she made a dramatic recovery, spoke rationally, and took fluids and biscuits in the evening, though very sluggish. The left leg was still hypertonic, with an extensor plantar response. She was continent of urine. The temperature was normal.

By Oct. 24 there were no abnormal signs in the nervous system, and she was allowed up in a chair.

When discharged fully ambulant on Nov. 2 she had no residual symptoms or abnormal signs.

Complement-fixation tests for influenza-A antibodies gave a titre of 1 : 64 on Oct. 21 and the same on Nov. 1.

Case 2.—A boy, aged 10, was admitted on the afternoon of Oct. 19. His illness had begun five days previously with a cough lasting two days, anorexia, and general malaise. On Oct. 17 vague abdominal pain developed, with bouts of vomiting which persisted. About five hours before admission he became drowsy.

On admission he was severely ill, unconscious, and restless. He responded sluggishly to painful stimuli but did not obey commands. There was no neck stiffness but Kernig's sign was positive. Tendon-jerks were all present and brisk. The plantar response was bilaterally extensor. Muscle tone was normal. Temperature 98°F; pulse-rate 110 per min.

The C.S.F. was clear and colourless, with no cells, protein 20 mg. per 100 ml., and no increase in globulin. No organisms were seen on the stained centrifugate and no growth resulted from subsequent culture.

An intravenous infusion of dextrose-saline and Hartmann's solution was given into the right leg and restlessness was controlled with paraldehyde.

On Oct. 20 his condition was unchanged, though he could swallow small quantities of water. His temperature did not exceed 99°F.

On Oct. 21 he made a dramatic recovery, returning to full consciousness within six hours. The plantar response became flexor. Lumbar puncture on Oct. 22 produced a clear fluid containing no cells, 15 mg. protein per 100 ml., and no increase in globulin. No organisms were grown. Blood-count 12,000 white cells per c.mm. (71% were neutrophils, 23% lymphocytes, and 6% monocytes).

When allowed up on Oct. 25 he was found to have a foot-drop on the right side with gross weakness of the anterior crural and peroneal groups of muscles. The distribution of the motor and sensory involvement was in keeping with a lesion of the lateral popliteal nerve. There was no other evidence of focal involvement of the nervous system.

Complement-fixation tests for influenza-A antibodies gave a titre of 1 : 4 on Oct. 21 and 1 : 16 on Nov. 2.

Discussion

These two children had a severe encephalitis after a relatively minor illness. Both passed into coma in less than twelve hours with extensor plantar responses and no significant abnormality in the cerebrospinal fluid. In case 1 there was evidence of focal signs in the nervous system on the left side of the body, but in case 2 there were no localising signs. After being gravely ill in coma (for three days in case 1 and thirty-six hours in case 2) both made a rapid recovery. The residual lesion of the lateral popliteal nerve in case 2 is hard to account for except as due to trauma; but there was no direct evidence of trauma to the nerve by splintage or otherwise in the course of the intravenous infusion.

The fourfold rise in titre in the complement-fixation test in case 2 indicates infection with influenza virus A. The initial high titre in case 1 signifies a recent infection with influenza virus A (Stuart-Harris 1953).

The general course of the illness was very similar to that in children with influenzal pneumonia admitted during the present epidemic—namely, an acute illness lasting two or three days, with a fairly rapid onset and rapid recovery from the acute phase.

Neither child has had recent vaccinations or any of the illnesses known to cause encephalitis. The evidence favours a diagnosis of acute encephalitis due to influenza virus A rather than sporadic encephalitis happening to coincide with an outbreak of influenza (Stuart-Harris 1953).

I am grateful to Dr. David Lawson for permission to report his cases, and to Dr. G. T. Stewart (pathologist to the hospital) and the Public Health Laboratory, Colindale, for the complement-fixation tests.

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PERFORATION OF THE COMMON CAROTID ARTERY BY A FOREIGN BODY IN THE PHARYNX

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MASSIVE hæmorrhage due to swallowed foreign bodies is most commonly caused by perforation of the aorta. Barrie and Townrow (1946) collected 80 such cases. Perforation of a major blood-vessel in the neck appears to be much rarer, and very few cases have been reported in recent years; but Schlemmer (1929) collected 29 cases up to that date, and in 17 of these a common carotid artery was involved.

The following case is unusual, and has several interesting features, not the least of which is that the patient recovered, thanks largely to a fortuitous circumstance that made the foreign body easy to remove.

Case-report

A married housewife, aged 51, was brought to hospital on Aug. 12, 1956, about thirty minutes after a severe hæmorrhage from her throat. She was in a collapsed state and her history was obtained partly from her husband and partly from herself when she had recovered somewhat. About four weeks previously, while she was eating her dinner, a lump of meat stuck in her throat. She pushed it down with her fingers but felt pain in her throat. Fearing that a fragment of bone might have become lodged she went to the casualty department of a local hospital and was reassured. Dysphagia persisted but improved over the ensuing few weeks. Suddenly, on the evening of admission, just after she had coughed, bright blood began to pour from her mouth, and shortly afterwards she fainted. The bleeding abated after an estimated loss of about two pints, and she was brought to hospital without delay. She was admitted to a medical ward because the bleeding was at first thought to be a hæmatemesis or a hæmoptysis.

She was pale and shocked, with temperature 97°F, pulse-rate 110, blood-pressure 100/40 mm. Hg, and an ill-defined firm swelling deeply placed in the left side of her neck. Physical examination revealed no other abnormality. Chest radiography showed normal lung fields.

Treatment and Progress.—Her general condition improved steadily with anti-shock treatment, including blood-transfusion, but during the ensuing twelve hours she regurgitated small amounts of altered blood at short intervals. The swelling in her neck appeared to diminish during this period. The amount of hæmoglobin in her blood eight hours after admission, by which time she had received two pints of blood, was only 48%. By this time it was clear that the hæmorrhage had come from a lesion in her pharynx or upper œsophagus, and a surgical opinion was sought. I first saw the patient fourteen hours after admission, and at this time, though pale, her general condition was satisfactory. The only abnormality was an elongated pulsatile swelling some 3 in. × 1 in. in the position of the upper part of the left common carotid artery.

Direct Pharyngoscopy and Œsophagoscopy.—Under general anæsthesia the pharynx was first inspected with a long laryngoscope. A thread-like structure lying against the posterior wall of the hypopharynx was grasped with forceps and pulled out. It proved to be a length of thread; and with it came a somewhat corroded sewing-needle $1^1/_4$ in. long, which had providentially remained threaded. After this there was no further hæmorrhage.

Postoperatively penicillin was administered for five days, and the patient made an uneventful recovery. The swelling in her neck disappeared within a week.

The patient recalled that, about a month previously, she had served a meal after she had been sewing. She thought that she must have put her needle into the front of her dress and that it must have dropped into the meat as she bent over to serve it.

Discussion

The diagnosis was not so straightforward as might be supposed, partly because the patient was unaware that she had swallowed the needle, and partly because she was too ill after the hæmorrhage to emphasise the amount of dysphagia she had had during the previous month. Chest radiography showed no abnormality in her lung fields, but reinspection of the film subsequently showed the needle clearly at the extreme upper end of the radiograph. When the wet plates were examined originally this part of the radiograph had been obscured by the frame carrying the film. The swelling in the neck was evidently a hæmatoma caused by bleeding into the tissues of the neck at the time of the original hæmorrhage. The regurgitation of altered blood during the twelve hours after admission was associated with considerable diminution of the hæmatoma, suggesting that it was discharging into the pharynx.

Perforation of a major artery usually follows the swallowing of a foreign body only after an interval of several days. In this case the interval was a month. Schlemmer (1929) explained this latent period by pointing out that a foreign body would not readily enter a mobile structure such as a large blood-vessel until that structure had become fixed by inflammation in its neighbourhood and, perhaps, softened by the same process. Continued pressure would then lead to gradual erosion of the vessel wall.

These was no evidence of sepsis in the present case, but it is certainly a factor of importance in some cases, such as that in which a foreign-body perforation of the wall of the right pyriform fossa had caused a parapharyngeal abscess (Thomson and Negus 1949). This had led to sloughing of the wall of the common carotid artery with fatal hæmorrhage. It is, however, quite possible for a sharp foreign body rapidly to penetrate the wall of the gullet and of a neighbouring vessel. Sneller (1936) described a woman who had sudden pain in the neck while eating chicken and rapidly developed a cervical hæmatoma. An impacted bone was seen on endoscopy but could not be removed, because blood obscured the field of vision.

Fatal hæmorrhage due to perforation of the œsophagus by foreign bodies is commonly preceded by a smaller warning hæmorrhage. If the possibility of a foreign body were considered in every case of bleeding from the pharynx or the œsophagus or of unexplained hæmatemesis, mistakes would be avoided, and timely operation might well save life.

Summary

Severe hæmorrhage followed perforation of the common carotid artery by a needle swallowed a month before. Removal of the needle was followed by an uneventful recovery.

I wish to thank Dr. J. W. Joule, under whose care this patient was admitted, for permission to publish this report.

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Preliminary Communication

TECHNIQUE OF HUMAN BONE-MARROW TRANSPLANTS

THE successful transplantation of bone-marrow in mice [1] and rabbits [2] after whole-body X-irradiation has revived hopes that bone-marrow could be satisfactorily transplanted in man.[3] The potential danger of whole-body irradiation, which is a hazard for all workers in nuclear irradiation, indicates the need to explore this possibility. We have attempted marrow transplantation in five cases and feel that the results may be of interest.

The Recipients

Four of the patients had advanced malignant disease and anæmia, with leucopenia or thrombocytopenia indicating grave damage to the marrow, confirmed by marrow examination. This precluded further radiotherapy. The fifth patient had aplastic anæmia after being successfully treated for carcinoma of the vocal cord a year previously.

The Marrow Suspensions

Donor marrow was obtained by multiple puncture of iliac crests of relations who had the same ABO and rhesus blood-groups as the patient and whose red cells were compatible with his serum. Four parts of the marrow aspirated were added to one part of sterile acid-citrate dextrose solution, and these suspensions were injected into the recipient as soon as possible after collection.

Administration

In three cases the suspension was introduced into the descending aorta, by catheterising the femoral artery (two cases) or the left radial artery (one case). In the fourth case it was introduced by percutaneous puncture of the abdominal aorta. In the fifth the suspension was injected intravenously. The reason for choosing the aortic route in cases 1, 3, 4, and 5 was that the pelvis and lumbar vertebræ had been deliberately irradiated in the previous fortnight to destroy the cells present and produce hyperæmia, thus providing a suitable site for the injected marrow.

The amounts of marrow obtained and injected were:

Case no.	Age (yr.)	Sex	Weight (kg.)	No. of donors	Volume injected (ml.)	No. of cells injected	No. of cells per g. body-weight ($\times 10^4$)
1	25	F	50	3	43	$1{\cdot}019 \times 10^9$	2·04
2	11	M	50	1	25	$0{\cdot}575 \times 10^9$	0·115
3	14	F	30	3	44	$1{\cdot}188 \times 10^9$	3·96
4	66	F	46	4	47	$1{\cdot}06 \times 10^9$	2·30
5	67	M	63	3	48	$0{\cdot}897 \times 10^9$	1·42

All the patients received prednisone 30 mg. daily both before and after the infusion of marrow.

Results

Case 1.—A woman, aged 25, with advanced Hodgkin's disease. On Nov. 5, 1956, 43 ml. of suspension was injected from a catheter into the aorta at the level of the 8th dorsal vertebral body. This produced no symptoms. No improvement followed. No evidence of the injected cells was found at necropsy 3 days later.

Case 2.—A boy, aged 11, with aplastic acute leukæmia and staphylococcal septicæmia. On Dec. 14, 1956, 25 ml. was injected intravenously. No untoward symptoms. No improvement noted. At necropsy 10 days later there was no conclusive evidence of injected marrow.

Case 3.—A girl, aged 14, with neuroblastoma with multiple deposits in skeleton and soft-tissues. On June 19, 1957, 44 ml. of suspension was injected by percutaneous aortic puncture. Patient died from retroperitoneal hæmorrhage after completion of this operation.

Case 4.—A woman, aged 66, with advanced lymphatic leukæmia had her pelvis irradiated to a skin dose of 2500r. Puncture of an iliac crest immediately before infusion showed no nucleated red blood-cells. On Aug. 13, 1957, 47 ml. of suspension was injected by catheterisation of a femoral artery at the level of L2. The patient tolerated this well and showed considerable clinical improvement. A month later nucleated red cells were readily seen in the iliac-crest marrow obtained by puncture. This patient is still alive, and the procedure appeared to improve her general condition very greatly. This patient is still alive (Jan. 9, 1958) and is in fair general health. Her leukæmic condition is unchanged.

Case 5.—A man, aged 67, with aplastic anæmia had been successfully irradiated for carcinoma of the larynx. His pelvis and upper femora were irradiated to a dose of 2800r (skin dose). This was followed by 15 mg. of nitrogen mustard ('HN2') as a single injection 48 hours before the infusion of marrow. This was to depress further the reticuloendothelial system. On Oct. 10, 1957, 48 ml. of suspension was injected by catheterisation of a femoral artery. This man feels better for the procedure. The white-cell count, which previously was 500 per c.mm., is now 1000–1500 per c.mm. A comparison of sternal and iliac marrow taken at the same time a month later shows more nucleated red cells (18·8%) in the iliac-crest specimen than in the sternum (9·2%). This patient died of bronchopneumonia on Dec. 9, 1957.

These results show that it is technically possible to inject marrow cells in man. It would be desirable to increase the amount injected. In this connection the use of marrow from ribs surgically excised for non-malignant conditions is being explored. In the two examples we have studied, suspensions containing more than $1{\cdot}5 \times 10^9$ cells were readily obtained from each rib.

In conclusion we wish to emphasise that this is purely preliminary work.

We are grateful to Sir Stanford Cade, Mr. E. Stanley Lee, and Dr. C. J. Gavey for permission and encouragement to treat their cases, and to Dr. B. Strickland, of the radiodiagnostic department, for his invaluable assistance.

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Medical Societies

MANCHESTER MEDICAL SOCIETY

Growth of Viruses

AT a meeting of the section of pathology on Dec. 11, Prof. H. B. MAITLAND said that the mechanism of reproduction of bacteriophage had been taken as a prototype of virus reproduction in general. The desoxyribonucleic acid (D.N.A.) of the phage alone entered the bacterial cell and determined the synthesis of phage D.N.A. and protein, which were organised at a later stage into morphologically mature phage particles. These particles were released by bursting of the bacterium. During the earlier part of the process of reproduction no infective phage was found in the cell, and this period had been referred to as an "eclipse phase".

The ribonucleic acid (R.N.A.) of tobacco-mosaic-disease virus played a similar role in the reproduction of this virus (T.M.V.). It determined the infective property of the virus and the nature of the lesions produced. The R.N.A. of one strain had been combined in vitro with the protein of another to make a hybrid strain of T.M.V. virus. Plants infected with such hybrid strains

had symptoms characteristic of the strain, providing the R.N.A. and the new virus produced as a result of infection corresponded in every respect with the R.N.A.-donor strain; R.N.A. could be extracted from T.M.V.-diseased plant material and was itself infective, causing characteristic symptoms and the production of new complete virus.

An alternative method of reproduction was by binary fission, as in bacteria and in certain rickettsiæ. The reproduction of animal viruses might be by binary fission, or it might be similar to bacteriophage with an eclipse phase as part of the process, but some intermediate form of reproduction might exist.

The psittacosis virus and other closely related viruses multiplied by developing large forms which increased in number by binary fission and later subdivided into the smaller bodies which were the naturally infective virus. Because of their method of division psittacosis and similar viruses were regarded as resembling the rickettsiæ rather than the viruses.

The vaccinia virus representing the "pox" group of viruses was next to the psittacosis group, and morphological studies of ultra-thin sections of infected tissue had not suggested reproduction by binary fission. Growth curves of vaccinia in the chorioallantoic membrane of the developing chick embryo, as well as in a number of systems of tissue and cells incubated in nutrient media in vitro, had been studied, but further work was required to elucidate the mechanism of growth of vaccinia virus.

Nucleic acid, which was itself capable of transferring infection to susceptible animals, could apparently be separated from tissue infected with meningoencephalitis virus and with eastern equine encephalomyelitis virus, and this seemed to bring these two animal viruses into line with bacteriophage and tobacco mosaic virus with regard to the role of nucleic acid in virus reproduction.

Reviews of Books

Rheumatoid Arthritis

CHARLES L. SHORT, M.D., WALTER BAUER, M.D., WILLIAM E. REYNOLDS, M.D. Cambridge, Massachusetts: Harvard University Press. London: Oxford University Press. 1957. Pp. 480. 55*s*.

THIS book is based on a study of 293 patients with rheumatoid arthritis at the Massachusetts General Hospital, who have been followed for at least twenty years. Findings were recorded on a predetermined plan and according to presenting symptoms and signs (which are compared with those of a non-rheumatoid control series). The patients' subsequent histories are analysed in great detail.

Tracing the evolution of the concept of rheumatoid arthritis, Dr. Short and his colleagues show that most previous students of arthritis have failed to distinguish degenerative from rheumatoid joint disease in published series of patients. The authors set out their own criteria for diagnosis, and while they have undoubtedly avoided previous pitfalls, it is a weakness of their otherwise excellent analysis that they have included under the heading of rheumatoid arthritis 44 patients with spondylitis, as well as 10 with psoriasis and arthritis and 3 with ulcerative colitis and arthritis. Most opinions (supported by the recent evidence of the specific agglutination tests for rheumatoid arthritis) would nowadays distinguish these conditions as separate diseases. Nevertheless this book is one of the most authoritative and comprehensive studies of rheumatoid arthritis yet published. It is in the highest tradition of medical scholarship and will remain a standard work of reference for many years.

Deafness, Mutism and Mental Deficiency in Children

LOUIS MINSKI, M.D., F.R.C.P., D.P.M., consultant psychiatrist, Royal National Throat, Nose and Ear Hospital, London. London: Heinemann Medical Books. 1957. Pp. 82. 12*s*. 6*d*.

THE difficulty of distinguishing between deafness and mental deficiency has only lately been appreciated. Many children whose disturbed behaviour had been attributed to mental deficiency have been discovered to be deaf and within the normal range of intelligence. The child who is both partially deaf and mentally retarded is particularly hard to assess. For the past five years Dr. Minski has been able to study such problems in the research unit for children at Belmont Hospital, and this small book summarises his experience and opinions.

He discusses the general aspects of the subject and gives the relevant clinical data, before describing the layout and staffing of the Belmont unit and the methods of assessment. Short notes follow on audiometry, electrophysiological methods of assessment, and psychological testing by the Drever-Collins and Merrill-Palmer tests. Although Dr. Minski is to be congratulated on drawing attention to the problem of the deaf who have been erroneously diagnosed as defective, he has by implication been of less service to the mental defective who is not deaf. Unfortunately in the first sentence of the first chapter he quotes the definition of the "feebleminded" child from the original Mental Deficiency Act of 1913, without reference to the amendments effected by the Education Act of 1944 relating to the "educationally subnormal" child. It is also disappointing to those who are trying to improve the training of mentally defective children for a note on the dust cover to refer to such children as those "for whom nothing can be done."

It is to be hoped that Dr. Minski will, in a second edition, amplify his theme by a more detailed exposition of clinical matters relating to deafness and also put into better perspective the problem of the mentally defective child, especially since the publisher has abbreviated the title on the cover to Mental Deficiency in Children.

An Introduction to Functional Anatomy

DAVID SINCLAIR, M.D., professor of anatomy, University of Western Australia. Oxford: Blackwell Scientific Publications. 1957. Pp. 426. 42*s*.

WHILE teaching at Oxford, Professor Sinclair lectured for some years at the Dorset House School of Occupational Therapy, and his new text is closely linked to the syllabus for occupational therapists, and for those with similar needs, such as physiotherapists. As is customary in such circumstances, anatomy and physiology are combined.

Like all who attempt simultaneous description of structure and function, Professor Sinclair meets difficulties. But though his book may appear at first sight to be divided into a first part largely dealing with function, and a final section actually entitled Topographic Anatomy, careful reading will show that in fact anatomy and physiology are far more closely interwoven than is apparent from the table of contents.

This bold attempt is on the whole successful. It is a pity though that the integration of the autonomic with the rest of the nervous system is not brought out more clearly. Some readers may wonder too whether the orthodox insistence on a primary protective function in the ribs is not medical rather than biological. The distinction is not made between primary cartilaginous joints and sutures, as growth mechanisms, and the true locomotor joints of the body. These are small criticisms, but in a book which in title puts the accent on function, such matters should be given more clarity than is usual in strictly anatomical texts.

The book ends with an excellent glossary and even a small bibliography. Illustrations are simple but adequate. In all it is a most readable work, which deserves and can be recommended to a far wider circle of readers than the one to which it was immediately directed.

The Respiratory Muscles and the Mechanics of Breathing

E. J. MORAN CAMPBELL, M.D., PH.D., M.R.C.P., assistant, department of medicine, Middlesex Hospital, London. London: Lloyd-Luke. 1957. Pp. 131. 20*s*.

THIS is a useful account of what is known of the action of the individual respiratory muscles and of their patterns of organisation.

The text is clear and without too much argumentation. Dr. Campbell freely admits that information is in places incomplete—for example, concerning the action of the internal intercostals. The arrangement of the last few chapters could perhaps be improved: it would surely be better to consider the force-volume diagram before considering what limits inspiratory and expiratory efforts. This would have revealed that the argument offered in favour of reflex limitation is largely circular.

We particularly hope that those concerned with the instruction of physiotherapists will read this book. Its guidance should help to remove much of the faulty thinking about breathing exercises that is at present so common.

Introduction to Anesthesia

The Principles of Safe Practice. R. D. DRIPPS, M.D., professor and chairman, department of anesthesiology, University of Pennsylvania; J. E. ECKENHOFF, M.D., professor of anesthesia, University of Pennsylvania; L. D. VANDAM, M.D., clinical professor of anesthesia, Harvard Medical School. Philadelphia and London: W. B. Saunders. 1957. Pp. 266. 33*s*.

THE appearance in recent years of many good monographs on particular aspects of anæsthesia has tended to detract from the value of more general books. It is satisfying, therefore, to welcome a book in which the fundamentals of anæsthesia are outlined in an intelligent way that will appeal to many readers. Precept and practice, especially at an elementary level, are apt to make dull reading, but Dr. Dripps and his colleagues have managed to blend them with a large amount of up-to-date and objective information. This is not in any sense a comprehensive textbook, nor is it intended to be, since such subjects as hypothermia and induced hypotension are omitted, but it is one of the best introductions to the subject yet published. British anæsthetists will find that its contents generally match the pattern of accepted teaching in this country.

Traquair's Clinical Perimetry (7th ed. London: Henry Kimpton. 1957. Pp. 333. 60*s*.).—Prof. G. I. Scott is to be congratulated on the added clarity which his judicious pruning has introduced into the text of this universally accepted guide to the technique of perimetry and the interpretation of defects of the visual fields. Some simplification of the early chapters on perimetric instruments and methods of examination has been achieved and will be especially valuable to those learning the art of quantitative perimetry. Of necessity, this leads to dogmatism in such matters as test objects and fixation devices; and though it would not command general agreement, the account of the Edinburgh technique is a useful guide. The fuller discussion of the applied anatomy of the visual pathways is welcome, and it is to be hoped that increasing knowledge—e.g., of the blood-supply of the optic nerve and chiasma—will enable this policy to be continued in later editions to include such fundamental data in even greater detail. The expansion and rearrangement of the section on optic-nerve lesions is also an attractive change. It now presents a clearer picture of the characteristic field changes in known types of optic-nerve disease and adds to these certain new lesions which recent reports have incriminated as responsible for optic atrophy. The decreasing clinical significance of tobacco amblyopia may not warrant so long a discussion. Now that the importance of optic-nerve disease as a blinding lesion is beginning to emerge, however, this chapter is of special value.

Medical Jurisprudence and Toxicology. (10th ed. Edinburgh and London: E. & S. Livingstone. 1957. Pp. 720. 47*s*. 6*d*.).—The new edition of Prof. John Glaister's famous Scottish textbook needs no introduction, for there can be few doctors who have not at some time turned to it for guidance. It is essentially a book of reference covering the whole of forensic medicine and toxicology. Since the last edition in 1950 several Acts of medicolegal importance, including the Homicide Act, Medical Act, and Sexual Offences Act, all of 1956, have appeared, and these are referred to in the text. The section dealing with the Poison Laws has also been revised in the light of fresh legislation.

This new edition, revised in collaboration with Dr. Edgar Rentoul, lecturer in forensic medicine at Glasgow University, maintains the traditional high standard of medicolegal exposition which has always been associated with its predecessors, and is an essential textbook for those who practise and teach the subject, both north and south of the border.

New Inventions

NEW BRONCHUS CLAMPS

NONE of the established types of bronchus clamps tried by me over many years has been satisfactory. All permit the bronchus to slip when under tension, except the spiked ones, and these are dangerous and often difficult to apply. They are all also too thick in the blade for lobectomy and segmental resection because they leave an inadequate stump for suture. Usually the angle of the blades on the handles is too obtuse except for pneumonectomy, and the long nose of the blades tends to catch the major blood-vessels in the lung hilum.

The principle of the Potts clamp with its multiple fine teeth enables these objections to be overcome. Therefore I have designed a set of three bronchus clamps, suitable in size and angle for pneumonectomy, lobectomy, and segmental resection.

These have been made for me by the Genito - Urinary Manufacturing Company, London, and for eighteen months I have used them only and with complete satisfaction. They are light, are easy to handle and apply, take up little room in the lung root, and do not slip. Being non-crushing, they have occasionally been applied deliberately to the proximal cut bronchus without prevention of its subsequent healing.

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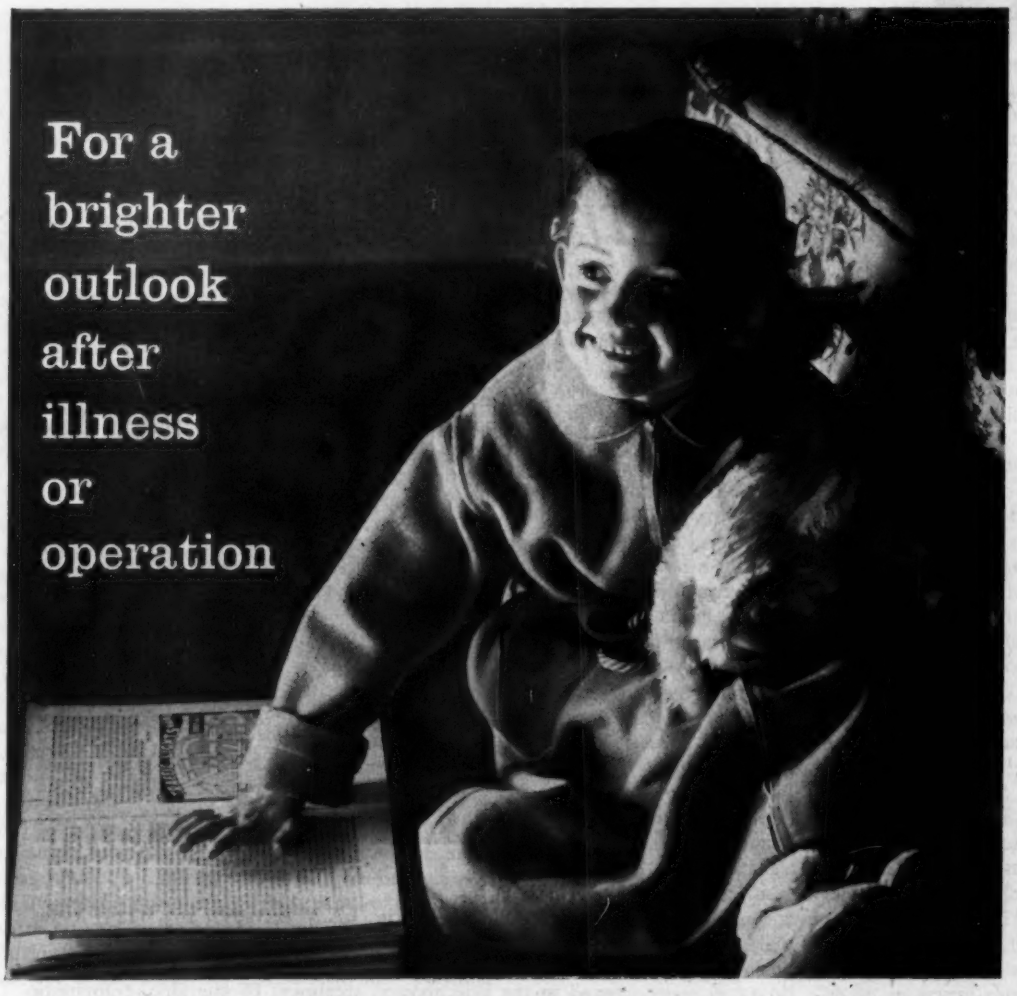

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THE LANCET
LONDON 18 JANUARY 1958

Diagnosis of Myocardial Infarction

MOST of us no doubt cherish the belief that our own diagnoses are usually right: if the truth were known, disillusionment might follow. In a recent analysis, for example, PATON [1] found a remarkably low level of accuracy in the clinical diagnosis of myocardial infarction, a common condition in which the clinical picture and electrocardiographic changes often leave little room for doubt. He analysed data from 266 postmortem examinations in a large teaching hospital during a period of two years. The results fell into three groups—those in which the diagnosis of myocardial infarction was confirmed, those in which it was disproved, and lastly a group in which death was due to myocardial infarction after some other diagnosis had been made. The clinical diagnosis of infarction was correct in only 118 (54%) out of 214 cases, and in a further 52 the diagnosis was not made before death. These bare figures give a misleading impression, since death was often sudden and the diagnosis little more than a guess based on probability. In these circumstances death was often wrongly attributed to pulmonary embolism. Profound shock, obscuring the clinical picture, accounted for the wrong diagnosis of 13 cases of pneumonia in which the patient died shortly after admission. Similarly, 12 patients who collapsed soon after surgical operations were thought to have myocardial infarcts, but in fact many died from hæmorrhage and in others no obvious cause could be found. Besides pulmonary embolism, many of the diagnostic pitfalls of the textbooks were evident. Rupture or dissection of the aorta was unsuspected in 7 patients, and once wrongly diagnosed during life. Only 2 abdominal emergencies were mistakenly thought to be examples of myocardial infarction. If profound collapse can obscure the clinical picture, cardiac failure, either left ventricular or congestive, can certainly do so, and patients who present in this way often have no pain.[2] PATON found 15 such patients in whom the diagnosis was missed, and he rightly emphasises that cardiac failure is not a diagnosis by itself, and that myocardial infarction should always be suspected in the absence of any other cause.

Electrocardiography is an extremely accurate guide in the diagnosis of myocardial infarction, and it is now usually agreed that a 12-lead electrocardiogram does not remain normal after acute infarction [3]: in case of doubt it should be repeated. But, although abnormal, the electrocardiogram may not be characteristic, and previous infarction, bundle-branch block, or a left ventricular "strain" pattern may all mask recent changes. Q waves may be absent unless the infarct is transmural, causing isolated T-wave changes to be labelled "non-specific". Though massive pulmonary embolism can simulate posterior infarction, the pattern shows significant points of difference.[3] In PATON's series it seems clear that electrocardiograms suggestive of myocardial infarction or damage were often ignored, and it was the physician who was proved wrong. Only 6 out of 97 electrocardiograms failed to show a recent infarct which was subsequently proved to exist, and 3 of these in fact suggested ischæmia. The remaining 3 showed left bundle-branch block. This accuracy of electrocardiographic diagnosis confirms the findings of FAILEY,[4] and ZINN and COSBY.[5] By contrast, the clinical diagnosis unaided by the electrocardiogram in 37 cases of myocardial infarction was correct in only 13 (35%). Here at least must we admit that machines are far less fallible than man.

The ideal biochemical test for myocardial infarction does not exist. The sedimentation-rate is raised in over 90% of patients with recent myocardial damage, but so it is in a host of other conditions. PHEAR and STIRLAND [6] found increased levels of C-reactive protein and plasma-fibrinogen in cardiac infarction, but normal levels in acute coronary insufficiency and severe angina. They regarded these two figures as sensitive indicators of muscle damage, and their estimation was relatively quick and simple. Unfortunately C-reactive protein and fibrinogen may also increase in various other conditions. The serum level of glutamic-oxalacetic-transaminase (S.G.O.T.) in myocardial infarction and ischæmia has been extensively studied [7 8]: this enzyme is present in high concentration in heart muscle, and is released after infarction in amounts proportional to the damage. If damage to the liver, skeletal muscle, pancreas, and kidneys, all sources of the enzyme, can be excluded, high S.G.O.T. levels suggest myocardial infarction. The level rises within forty-eight hours and stays up for three or four days. Inflammatory conditions do not lead to an increase in S.G.O.T., except in severe rheumatic carditis, and for some reason aspirin administration may give a false result.[9] It seems then that the S.G.O.T. level is the most sensitive and specific indicator of myocardial damage yet available, but clearly it has its drawbacks, like any other biochemical test. There has been some argument as to whether S.G.O.T. levels are raised in pulmonary embolism,[7] and in acute coronary insufficiency, and it is important to establish the facts here. Estimation has hitherto been unsuitable for routine work, but the newer colorimetric methods are proving quick and reliable.[10] While the electrocardiogram will usually provide the answer, it seems reasonable to hope that S.G.O.T. estimation may prove a valuable aid when the findings are equivocal.

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Suburban Neurosis Up to Date

IT is now nearly twenty years since TAYLOR[1] described in our columns a condition which he called "suburban neurosis". He was writing about life in the new housing estates which had sprung up round our great cities. In these estates—sometimes jerry-built and almost always devoid of social amenities—it was considered correct to keep oneself to oneself. The one-child family and the baby car represented the height of ambition; and, though physical health was comparatively good, many of the people had anxiety states, often with hysterical features and reactive depression, which TAYLOR attributed to boredom, loneliness, and a false set of values. One of the happier results of the 1939–45 war, and particularly the continuing threat of air-raids, was to build a new community life in such places. Fire-watching, the Women's Voluntary Services, evacuation, and many forms of mutual help broke down the previous social isolation, and the prevalence of neurotic illness declined spectacularly. Afterwards there was some slipping back, but the social isolation of the inter-war years has not been fully restored.

Since the war, the emphasis of building development has changed. Green belts of a sort have been established around the cities, and instead of the speculative hire-purchase estates we have had huge blocks of municipal flats, large out-county municipal estates, and the new towns. (Only within the past three years has speculative building recommenced, and its scale is much smaller than before.) Though redevelopment in municipal flats has had its social difficulties, old ties of friendship and kinship have not been broken, as must happen when a family moves right out of the city. In the new towns, industry and homes have moved out together, and imaginative social provision has done much to reduce the risk of neurotic reactions in a new environment—though the combination of high rents, hire-purchase payments for furniture, and rapidly increasing families often leads to justifiable financial anxiety.[2] The out-county municipal estates, however, have long been suspected of partly repeating the story of the pre-war speculative estates. Great working-class populations were translated to new homes in country suburbs; and, though the standards of housing were admirable, social provision was at first very meagre: the great majority of the wage-earners continued to earn their living in London, while the women tended to follow the obsolescent middle-class pattern of social isolation as a standard of respectability. Hence it was good that a team from what was then Prof. J. M. MACKINTOSH's department at the London School of Hygiene should decide to make a detailed study of what was going on in one of these out-county estates to the north of London. Two reports of this team's work appeared last year,[3 4] and a third, by MARTIN, BROTHERSTON, and CHAVE,[5] deals with the incidence of neurotic and psychotic illness.

Four sources of information were tapped—mental-hospital admissions, referrals to psychiatric outpatient clinics, general-practitioner consultations, and the results of a direct-interview survey. Between 1949 and 1954, there were 129 admissions to mental hospitals from the estate, giving a rate slightly more than 50% above what would be expected from national figures. Admissions for neuroses were twice the national rate, with neurotic reactive depression among females predominating. On the other hand, the discharge-rate was high, and the average period in hospital short. Psychiatric outpatient referrals did not differ markedly from the national average, but were twice as numerous as in neighbouring areas served by the same hospitals. During 1953, all the doctors in general practice on the estate maintained records of all their consultations, and the following table shows the number of patients consulting them for various complaints (per 1000 registered population) set alongside "expected" figures:

Diagnosis	*Actual estate figure*	*Expected estate figure on national basis*
Psychosis	3·0	1·0
Anxiety neurosis	23·4	11·8
Disturbances of sleep	25·6	6·3
Anorexia	9·7	2·1
Palpitations	1·1	0·2
Debility and undue fatigue	50·9	13·3
"Depressed" or depression	7·0	3·3
Headache	29·6	10·0
Urticaria and allergic rash	24·8	19·5
Duodenal ulcer	10·2	3·9
Asthma	12·1	7·6

The direct-interview survey showed that the self-estimate of "nerves" on the estate was 223 per 1000 adults, compared with the national figure of 126 obtained by the Social Survey of Sickness.[6] Complaints of neurotic symptoms were higher among those who had lived on the estate for two years or less than among those who had been there for three to six years; but even the oldest inhabitants had rates far above the national figures. Admittedly, rehousing on an out-county estate is partly determined by medical certificate; but a psychiatric or quasipsychiatric diagnosis had been submitted for only 2% of men and 8% of women, and these can account for only a small part of the excess of neurotic illness encountered.

Here, then, is the suburban neurosis presenting itself again, and probably for much the same reasons. As Professor BROTHERSTON and his colleagues remark, each family "keeping itself to itself" generates a degree of loneliness and social isolation inconsistent with good mental health. The findings at direct interview and the statistics for juvenile delinquency suggest that, with time, there is a slow improvement; but the picture remains a sad one. Physical planning on the out-county estates appears to be out of step with social planning, and rehousing has improved physical environment at the cost of mental wellbeing. There is reason to think that in the new towns the lessons of the past have been learnt and applied. Precise statistical evidence has yet to be collected, but we agree that "comparable studies of mental health problems in New Towns . . . would be especially

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5. Martin, F. M., Brotherston, J. H. F., Chave, S. P. W. *Brit. J. prev. soc. Med.* 1957, **11**, 196.
6. Stocks, P. Studies of Medical and Population Subjects, no. 2. H.M. Stationery Office, 1949.

illuminating". The present study supports the view that social environment affects the prevalence not only of neurotic but also of psychotic illness; and, if this is so, the future of preventive psychiatry will lie as much in social planning as in early diagnosis and treatment. A few thousands of pounds spent on social amenities and social development may save hundreds of thousands used on therapeutic services or wasted in labour lost.

Artificial Insemination

ARTIFICIAL insemination of livestock is now widely practised, and its techniques are both simple and reliable. There are few practical difficulties in carrying out the same process in human beings; and most of what has been written on this subject turns on the desirability of doing so. In a new review [1] of the human applications of the method, a Dutch obstetrician and gynæcologist deals with both types of insemination now in use—from the husband and from a donor or donors. He discusses techniques, but he is more closely concerned with far more contentious matters. Few biological discoveries trespass on so many sensitive areas of human belief, and the body of resulting comment—legal, religious, and ethical—is the main topic of Dr. SCHELLEN's review. For some commentators every stage of the process, from the manner of collecting semen and the desirability of paying the donor to the risk of inadvertent marriage between siblings, is of immediate and serious moral importance. Others are more preoccupied with the effects on parents, child, and doctor of granting or refusing a request for donor insemination. In the discussion of these possible effects, rationalisation often plays a recognisable part. SCHELLEN does not wholly escape the charge of special pleading in his chairmanship of the debate, and his *parti pris*, although evident, is overtly declared only in his last few pages. But his book is a fascinating study of the social anthropology of human opinion.

Such an alarming battery of theological, moral, magical, psychological, and admonitory comment is likely, thus presented, to deter any cautious doctor from involving himself, at least in donor insemination; and the deterrent action was perhaps SCHELLEN's aim. Many whose ethics are based on similar religious belief may well agree with his assessment and emphasis. To others, it may seem that patients seeking medical help in their desire for children are less agitated by scruple over details of procedure than are their spiritual mentors. At the same time, the possibility of all kinds of trouble arising from donor insemination must be evident to all but the blindly sanguine. SCHELLEN quotes many such forebodings; the actual failures he mentions are largely anecdotal. But his book poses once more one of the central questions of medical ethics—how the moral and religious opinions of the doctor and his patient should determine the advice given in matters of conduct.

He offers only conjecture on the motives which lead patients to request donor insemination. These are important and probably diverse: it would be possible to take the extreme position that well-adjusted patients will not require donor insemination, and the ill-adjusted may be harmed by it; such a view leads, at least, to dignified inactivity. Some doctors believe that donor insemination has a valid place in medical practice, and meets both a demand and a right. There are those who would no doubt agree with GUTTMACHER,[2] both in his summary handling of the theologians and in his general advice—that the doctor should act on his judgment and knowledge of the patient, with privacy and without formality of any kind, avoiding the formidable legal instruments prepared by some authorities bent on self-protection, refusing high fees, and " putting the name of the husband as father on the appropriate forms—a white lie here is a humane, friendly deed ". At the opposite extreme, there is anxious debate whether a donor who accepts payment is morally fit for fatherhood, or whether he is entitled to demand it for " a service more distasteful than that of a blood donor ". Even the use of the husband's semen gives rise to heart-searching in some places. Every approach, from an ingenuity of scruple worthy of *Hudibras* to frank commercialism, is cited in SCHELLEN's collection: the only criticism of its scope is that this citation of extremes leads to an under-representation of more moderate judgments.

Since many critics of artificial insemination base their objection, at least in part, on genetic and psychological risks, it is unfortunate that we have here no follow-up studies of couples who have borne a child in this way, and no serious discussion of the biological implications in terms of modern genetics. Evidence of this kind might form a more manageable basis for advice than appeals to general, or even infallible, moralities. The genetic comment is uncritical, both in exaggerating by implication the physical consequences of accidental endogamy, and in accepting anecdote—about supposed man-ape hybridisation, for example. There are those who will read Dr. SCHELLEN with irritation; but the human anxieties he writes of are real and deepseated, even when unspoken. Mountains of this kind have to be scaled by the patient, even when they have been made from what, to the unconvinced sceptic, appear to be ethical molehills. Some of the instances of medical insensitivity to which SCHELLEN refers are warnings against overconfidence and undue persuasion.

Eradication of Malaria

MALARIA eradication, though known to be feasible, might have been pursued only exceptionally but for the fear that, owing to the growth of anopheline resistance, control by means of residual insecticides could not be maintained permanently. The W.H.O. Expert Committee on Malaria, in recommending eradication,[3] points to its social and economic advantages, and remarks that it needs special finance for a limited time only. Moreover, in achieving eradication a government gains an asset in well-trained staff available for other services.

1. Artificial Insemination in the Human. By A. M. C. H. SCHELLEN, M.D., resident at the department of obstetrics and gynæcology, University Hospital, Groningen. New York: Elsevier. London: Cleaver-Hume. 1957. Pp. 420. 72*s*.

2. 2nd American Congress of the Society for the Study of Sterility, 1942.

3. *Wld Hlth Org. techn. Rep. Ser.* 1957, no. 123, p. 5.

Annotations

INFLUENCE OF ACID-BASE BALANCE ON THE ACTION OF DRUGS

CHANGES in acid-base balance have long been known to influence both the therapeutic and toxic effects of salicylates. Administration of sodium bicarbonate reduces the toxicity and plasma level of salicylate [1]; and Smith et al.[2] showed that this was due to increased rate of excretion of salicylate in alkaline urine. The clearance of unconjugated salicylate is much lower than that of inulin in acid urine, but is higher in alkaline urine.[3] Hyperventilation and acetazolamide, both of which produce an alkaline urine, are as effective as sodium bicarbonate in increasing salicylate excretion.[4] Since acetazolamide produces systemic acidosis,[5] the increased salicylate excretion in alkaline urine must be directly related to the urinary pH and not to change in systemic acid-base balance.

More recently the excretion of two other important drugs, phenobarbitone and mecamylamine ('Inversine'), has been shown to resemble that of salicylate. Phenobarbitone, which is a weak acid, is excreted more rapidly when the urine is alkaline.[6] Barbitone itself, although also largely eliminated in the urine, is little affected by variation in acid-base balance. Mecamylamine, a weak base, is excreted more rapidly when the urine is acid.[7–9] Other ganglion-blocking drugs, such as hexamethonium and pentolinium, are much stronger bases and are unaffected by acidosis or alkalosis. Many other weak bases, including mepacrine and chloroquine,[10 11] procaine,[12] and quinine,[11 13] are excreted in the same way as mecamylamine. Variation in excretion-rate in the case of the weak-base drugs is, however, of little importance since only a small proportion of any dose appears in the urine. Alkalinisation of the urine increases the hypotensive effect of mecamylamine,[8 9] and reduces the toxicity of phenobarbitone and salicylate. Acidification of the urine by ingestion of ammonium chloride has the opposite effect. Treatment with sodium bicarbonate has been recommended both in salicylate [4] and in phenobarbitone [6] poisoning. Other workers have recommended dialysis with the artificial kidney in salicylate [14] and barbiturate [15] intoxication. Probably the ideal method of removing the drugs from the body in severe poisoning is a combination of the two methods.

Variation in the rate of excretion of these drugs influences the amount retained in the body, and therefore there is a gradual modification of their pharmacological effects. In contrast, sudden changes in systemic acid-base balance may rapidly alter the distribution of drugs within the body, while the total amount remains unchanged. This may be associated with corresponding change in their specific action. Respiratory acidosis induced by breathing 10% CO_2 increases the plasma levels of the bases mepacrine and chloroquine [16] and of mecamylamine,[17] but reduces those of the acids phenobarbitone [6] and thiopentone.[18] Except in the case of thiopentone, this is associated with a reverse change in the intracellular concentration of the drugs. Thiopentone is largely stored in adipose tissue, and in this case acidosis causes mobilisation of the drug from body fat.[18] An increased plasma level caused by acid-base change increases the pharmacological effect of mecamylamine,[17] but reduces that of phenobarbitone.[6] This observation may be of considerable practical importance during anæsthesia.

VIRAL HEPATITIS

VIRAL hepatitis remains common, and, though mortality rarely exceeds 0·2–0·5%, the illness may be long and unpleasant and permanent hepatic damage the final result. Large epidemics are fortunately rare, but under conditions of war or civilian catastrophe big outbreaks have been common during the past two centuries. The disease has been intensely studied in recent years, and it was the subject of a symposium at the last annual meeting of the American Medical Association. Advances in treatment have unfortunately been trivial, but some progress in the understanding of ætiology and epidemiology has been achieved and was well reviewed at the symposium by Havens.[19]

The two varieties of the disease are distinguished mainly by the route of infection and the incubation period. The causal agent of the naturally acquired disease (infective hepatitis) can be demonstrated during the period of infectivity in the blood-stream as well as in nasopharyngeal washings and in the fæces. The second variety of the disease has been given the name "homologous-serum jaundice" and the causal agent has been found only in the blood of patients and never in the pharynx or fæces. This second variety is transmitted only as a result of artificial procedures—e.g., blood-transfusions or injections given with an imperfectly sterilised syringe. Transmission of infective hepatitis, on the other hand, is usually by close personal contact or by fæcal contamination of food or water; but, since the virus is also present in the blood-stream at least for some days or weeks, it can also be transmitted in the same way as homologous-serum jaundice.

The viruses responsible for these two diseases belong to the class of filter-passers, and they are both remarkably resistant to chemical and physical methods of sterilisation. The relationship between them remains an intriguing problem. The coincidence between outbreaks of hepatitis among patients attending venereal-disease clinics for arsenical therapy and the presence of an epidemic of infective hepatitis in the same locality suggested a close connection between the viruses.[20] But the fairly consistent and striking difference between the incubation periods of the two forms of the disease and the difference in the distribution of viruses in the infected person rules out the possibility that the viruses are identical. This conclusion is firmly supported, moreover, by two further pieces of

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17. Payne, J. P., Rowe, G. G. *Brit. J. Pharmacol.* 1957, **12**, 457.
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evidence. Firstly, the agent of infective hepatitis confers a strong and lasting immunity against reinfection by infective hepatitis, without apparently enhancing the resistance to the serum jaundice. Secondly, an injection of normal adult human gamma-globulin gives considerable protection against infective hepatitis but is without demonstrable effect against the other form of the disease. Nor can these differences be entirely attributable to the different routes of infection, since parenteral transmission of infective hepatitis results in a disease with the characteristic short incubation period and the appearance of the virus in the throat and fæces. The conclusion, therefore, that virus hepatitis may result from infection by either of two immunologically distinct agents seems well founded. Their usual mode of transmission is equally distinct and well established, and the prophylactic measures are plain. All that is required, therefore, to reduce the incidence of this disease is their widespread and meticulous application. As Dr. Morton remarks in a letter on p. 164, efficient syringe sterilisation and a scrupulous injection technique are more than ever important at present, when large programmes of prophylactic inoculation are about to be carried out.

FAILURE TO GAIN WEIGHT IN INFANCY

IN a recent symposium on the relationship between pædiatric disorders and nutrition, Holt [1] discusses excessive loss of nitrogen from the body as a cause of failure to thrive in infancy. Cystic fibrosis of the pancreas is one condition in which there is abnormal fæcal loss of nitrogen; and in malignant malnutrition, or kwashiorkor, this fæcal loss is augmented by losses through the kidney. It seems likely that in kwashiorkor both digestive and tissue enzymes are deficient, so that much of what little nitrogen is absorbed cannot be used and escapes in the urine. Holt also draws attention to the need for caution in the treatment of patients with protein starvation. High levels of non-protein nitrogen have been found in the blood of patients with kwashiorkor who were taking protein by mouth,[2] and toxic effects have followed intravenous feeding with hydrolysed protein or amino-acids.

Careful investigation of most cases of "marasmus" will often reveal some obvious cause such as a congenital abnormality of the alimentary tract, heart, or nervous system, or perhaps an unsuspected infection. On the other hand, much elaborate effort may be needed to uncover certain metabolic anomalies. The symposium gives up-to-date information about such disorders as infantile renal acidosis, idiopathic hypercalcæmia, and galactosæmia, and refers to the various types of aminoaciduria. In these and allied disorders, the metabolic anomaly may exert its effect largely through impairment of appetite, and calorie losses in the excreta are unlikely to be large unless there is an accompanying glycosuria.

Holt also refers to a further group of children in whom there is a discrepancy between the amount of food the child is thought to be taking and the amount he actually receives. The difference may be the result of inaccurate or careless preparation of feeds, rumination or unreported vomiting, or, on occasion, downright deceit. Such children are often said to be suffering from "mismanagement" or "psychological upset"; and a spell under close observation in nursery or hospital may disclose a steady weight gain even though the food intake is apparently no different from that given at home.

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PRESSURE GROUPS

TODAY the words "pressure group" often drop off the journalist's pen or the orator's tongue; and to most readers and listeners they suggest yet another disagreeable development of the modern world. But this reaction is often unreasonable; for it is the name rather than the device that is novel. Runnymede, for instance, was the scene of one effective pressure group; and such reforms as the abolition of slavery, the Factory Acts, and (in more modern times) equal pay for women were all initiated by small groups of people, who, by exerting pressure, gradually brought the Government and the public round to their way of thinking. Nevertheless, though they can thus claim respectable ancestry and good service in the past, pressure groups, like other useful institutions, are changing with the changing times, and their new name is perhaps a sign of the community's uneasy recognition of their growing importance and power. The part they are now playing in the political life of the nation is examined with discernment and tolerance in the current issue of the *Political Quarterly*,[1] where the social scientist as well as the politician will find much of interest.

As the machinery of government has changed, so have the methods of the pressure group. The Runnymede group was small, and its methods direct and swift; but in a parliamentary democracy they would be less effective. New means of communication and ease of transport have given the modern pressure group new opportunities, but literacy and universal suffrage mean that it must convince more people if the climate of opinion is to be altered. The multiplication of pressure groups has in part been fostered by the Government's pervasion of the life of the citizen. To the courts of justice, the Army, and the Navy, for which the State has long been responsible, have been added such diverse enterprises as schools, roads, hospitals, pensions, mines, postal services, and museums, and each addition has provided a focus (or indeed foci) for several pressure groups. The Association of the ex-Bowmen of Agincourt, for instance, may have met annually on St. Crispin's day; but, unlike the ex-Service associations of our own time, it probably did not press the pension claims of its members.

Among these new groups the most conspicuous are the innumerable vocational ones formed by workers, whether members of a profession, traders, or artisans; and Sir Winston Churchill, with his historian's outlook, has perceptively described the trade unions as "an estate of the realm". While some of these are profoundly concerned with the public interest, others are concerned mainly or entirely with the interest of their members.

Besides these, however, there are still the groups whose sole purpose is to work for a cause—the legalisation of abortion or the abolition of capital punishment, to take two topical examples. True to their traditional pattern, most of these groups are small, with meagre funds; but their influence cannot be measured by their size or their finances, and it is largely through the kind of enlightened and disinterested pressure they exercise that so many wrongs have been righted by persuasion and that British history records so few revolutions. Unfortunately today the small ill-financed pressure group may be somewhat at a disadvantage, for publicity has become a more expensive commodity: to reach the public's ear and eye usually costs money, while competition for the public's mind and interest is keen. It is indeed perhaps

1. *Political Quarterly*, January-March, 1958.

a sign of this competition that the Government are themselves beginning to use some of these groups as a means of exerting pressure on the public. The subsidies which they offer to bodies such as the Marriage Guidance Council and the National Association for Mental Health are too modest to sap independence, but here is a development which may well initiate yet another morphological type of pressure group.

In many ways the growth of pressure groups, in number and influence, is a healthy sign: the device is one which can be used, with typical British economy, either as a spur or a bridle for the Government of the day. But with the shifting emphasis of these groups, their growing power, and the preoccupation of so many of them with the rights of limited sections of the community rather than the propagation of ideas and principles, it is essential that the rights of those who are prevented from forming groups, whether by isolation, ill health, youth, or age, shall not be neglected. The best of our pressure groups have always been created for the protection of the weak; and, despite all the changes time brings, their true strength will probably always lie in their readiness to recognise where help is most needed.

ATOMS, BRONCHITIS, AND CLEAN AIR

THE Windscale accident drew public attention to the risks of the civil use of nuclear power; but these risks are at least foreseen, as the report of the Fleck Committee (summarised on p. 157) illustrates. To quote the medical officer of health for Wigan,[1] "if the approach to the first industrial revolution had been as carefully and painstakingly controlled as regards the possibilities of environmental hazards to mankind as is the approaching Atomic Age we should now be a much healthier nation".

Nuclear power may in due course help to remedy some defects by freeing us from the need to burn coal in great quantity and so lessening the damage, to ourselves and our buildings, that comes from air pollution. We may hope that, before very long, smoky grimy industrial towns, and their coughing citizens, will be as distant memories as the London cholera epidemics are now.

Some measure of the havoc caused by the wastes poured into the atmosphere in industrial towns is given in a recent review of bronchitis in Salford.[2] In the years 1946–55 the death-rate from bronchitis per 100,000 population in England and Wales ranged from 55 to 84; in Salford the range was 114 to 178. (The death-rates from pneumonia, pulmonary tuberculosis, and lung cancer were all higher in that smoky city than in England and Wales, though the differences were less striking.) This implies that the death-rates from bronchitis are very high in Salford—not that they are low in England and Wales: in fact they are about 3 times those of Belgium, 6 times those of Germany, 15 times those of France and Scandinavia, and 36 times those of the United States. Chronic bronchitis may well now assume the mantle of the vanishing rickets and be called "the English disease". "Men in England awaking and clearing their bronchi before setting out to work make a fearful noise"[3]; and in 1956, bronchitis accounted for 5·6% of all the deaths in England and Wales (11·9% in Salford). Moreover, it is the cause of about a tenth of all the days lost from work through illness; and it cost the National Insurance Fund £7¾ million in one year.

Admittedly no certain link has been established between air pollution and bronchitis or other respiratory disease, but the epidemiological evidence is very strong.[4–7] Smoking aggravates bronchitis, and fog, temperature inversion, and influenza precipitate a rise in the number of deaths (the relationship with influenza epidemics may partly account for the tendency of the death-rate from bronchitis to rise and fall in alternate years). Clean air may come, one day, as a by-product, when nuclear fusion provides most of our power; but many years may slither away before then. To use the prospect as an excuse for inaction will cost very many lives and much misery. We may wish that our ancestors had not left us with such a legacy of inefficient smoke-emitting devices, but, to quote Dr. Hilditch [1] again, "we must make the best of the situation as it exists and improve our environment whenever and wherever we can."

The Clean Air Act lays on local authorities much responsibility for making these improvements, and we hope they will do more than they have yet done [8] to make use of their splendid opportunities of improving our health. The fact [2] that the bronchitis death-rate in Japan fell from 44·8 per 100,000 in 1947 to 9·9 in 1955 is both an example of what can be achieved and a stimulus to inquiry as to how it was done.

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7. Roberts, L., Batey, J. W. *Lancet*, 1957, i, 579.
8. See *ibid.* Jan. 4, 1958, p. 57.

NINETY

IN deciding when to publish an article, we seldom make any serious effort to ensure that it shall appear on the author's birthday. But we felt that an agreeable adventitious flavour would be given to Sir Leonard Rogers' latest contribution if we kept it for this week. For he was born on Jan. 18, 1868.

We must wait another ten years before asking Sir Leonard the routine question about the reason for his exceptional longevity; but the explanation certainly cannot be an inactive life. His astonishing output of original work comes of a combination of native wit with intense labour. His strenuous application to the matter in hand, from his earliest days in medicine, seems to have preserved, instead of impairing, a youthfulness of mind which still enables him to rely on his remarkable memory for detail when he speaks, without notes, on medical subjects. Regarding him as a contemporary, we may find it hard to remember that this is the man who introduced emetine for amœbiasis, antimony for kala-azar, and chaulmoogra preparations for leprosy, and who revolutionised the treatment of cholera before he turned his mind to the forecasting and prevention of this devastating disease, on which he is again making important practical proposals. Because he is so keen, he has a persuasive habit which gained from many sources large funds for the Calcutta School of Tropical Medicine and later for BELRA—the British Empire Leprosy Relief Association. His work has been his passion, and his conversation, as eager and rapid as ever, is of his work, his ideas, and his sons. He speaks as he is, a leader of thought and action; but he is never pompous, and his humour remains. He has enjoyed his life, as his autobiography *Happy Toil* makes very clear, and we wish him many more years in which he can use his genius to stimulate his juniors.

Special Articles

FORECASTING AND CONTROL OF CHOLERA EPIDEMICS IN SOUTH-EAST ASIA AND CHINA

Sir LEONARD ROGERS
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FORMERLY MAJOR-GENERAL, INDIAN MEDICAL SERVICE

IN a recent paper (1957) I recorded a tenfold reduction in the cholera mortality during the decade 1946–55 in the extensive endemic area of Lower Bengal—the home of cholera—together with a forty fold to fifty fold reduction in the more extensive epidemic areas of India, including the practical elimination of the disease in the Punjab and North-West Frontier provinces.

This unprecedentedly rapid decline in cholera mortality coincided with the general adoption of my suggestion of 1926 and 1928 to inoculate compulsorily the 20 million or so pilgrims, whom I had shown to have played a predominant part in disseminating cholera every year in epidemics over India, and in exceptionally bad years as pandemics over Asia and Europe, &c., during the 19th century.

During the fifteen years 1941–55, about 300 million people were inoculated against the disease in India, but during the first five of these years the second world war led to shortage of food and famine conditions; which are always accompanied by a greatly increased cholera incidence, due to widespread movements of the people in search of food. These circumstances prevented the full effects of the new plan of control being obtained during 1941–45. The continued use of the new measures during the decade 1946–55 doubtless had a cumulative effect. It should be noted that they have still to be tested after widespread failure of the monsoon rains, with inevitable increased cholera incidence (Rogers 1928, pp. 27–40). It is, however, a hopeful sign that after a failure of the north-east monsoon rains in the last quarter of 1936, the increase of cholera in South-East Madras was a comparatively mild one.

The success of control measures in India led me to extend my epidemiological inquiries to the incidence of cholera during the first half of the present century in South-East Asia and China, in the hope of extending preventive measures over these areas.

It was first necessary to establish the areas where the disease is endemic at all seasons of the year because the monthly absolute humidity (i.e., the mean water-vapour pressure) does not fall below the critical minimal point of 0·400 in. Hg during the winter months, as I showed to be the case in India (Rogers 1926, 1928).

The table shows that in Burma, Thailand (Siam), and Indo-China the lowest early absolute humidities of January and February remain above 0·400; so these are endemic areas. Burma is continuous with the endemic areas of Assam and the eastern provinces of Greater Bengal, from which cholera epidemics spread yearly over North-West and Central India, coincidently with the spring rise of the monthly absolute humidity to well above 0·400. The combined endemic areas of Bengal and South-East Asia, as defined above, are indicated by the hatching in the map (fig. 1).

On the other hand, China is a huge epidemic area in which the winter absolute humidities fall well below the critical line of 0·400 from November to March from the Yangtse valley northward, as shown by the monthly data of Shanghai near the mouth of the Yangtse river. The readings for the southernmost part of China, as illustrated by those at Hong Kong (in December, January, and February 0·405, 0·390, and 0·387 respectively) are on the borderland of the critical point. Southernmost China thus corresponds to the eastern sub-Himalayan North-West province of India (Rogers 1928 map VIII, p. 222) in being a borderland area where cholera is reduced to very small proportions during the winter, but recrudesces in March with the rise of the absolute humidity to over 0·400. Later the cholera spread farther to the north-west with the rise of the absolute humidity to well over 0·400 just as it does over Central and Northern China in epidemic years.

It was therefore necessary to study the annual incidence of cholera in South-East Asia, its possible connection with the Bengal endemic area to the west, and the spread north over China in epidemic form. For that purpose the available data from 1900 to 1955 have been collected, and the annual death-rates per 1000 are shown in the chart (fig. 2), so as to be comparable for India, Burma, Thailand, and Indo-China. The chart also shows the years in which epidemics of cholera spread over China, of severity graded I, II, or III (Wu Lien-Teh 1932).

Grade III includes the most serious epidemics, in which the disease spread over nearly all China as far north as Manchuria and Korea. Grade-I epidemics were limited to South China, and grade-II were intermediate, with involvement of Central China and the Yangtse valley. In the remaining years there were no widespread outbreaks, and only a small mortality from the disease in the extreme south of China, bordering on the endemic area of Indo-China, and in ships coming from southern endemic areas.

The Spread of Cholera from India to Eastern Asia

Before the data shown in the chart are considered, a brief summary must be given of the spread of cholera over Far East Asia in pandemics during the 19th and 20th centuries.

The earliest was recorded in the latter part of the 19th century by John Macpherson (1872). But the most striking was that of 1840–49, described by N. C. Macnamara in his classical *History of Asiatic Cholera* (1876), and illustrated by a map in my *Cholera and its Treatment* (Rogers 1911). Cholera was then carried by sea to China, and spread inland across Central Asia to reinvade the Punjab from the west and Upper Burma from the north, contrary to the general rule. The 1861–62 pandemic was also carried by the sea route to overrun China.

Since the endemic areas of Assam and Bengal are contiguous with Upper and Lower Burma respectively, we must study the

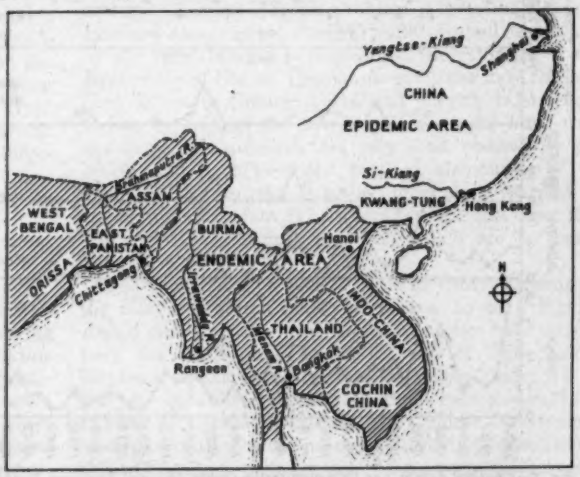

Fig. 1.—Map of endemic and epidemic areas.

MEAN MONTHLY VALUES OF WATER-VAPOUR PRESSURE (IN. HG)

—	January	February	March	April	May	June	July	August	September	October	November	December
Rangoon (Burma)	0·576	0·618	0·704	0·803	0·900	0·905	0·900	0·900	0·900	0·898	0·780	0·622
Bangkok (Thailand)	0·691	0·839	0·909	0·954	0·992	0·969	0·942	0·963	0·954	0·915	0·851	0·688
Hanoi (Indo-China)	0·413	0·499	0·561	0·747	0·907	0·977	0·977	1.022	0·918	0·726	0·620	0·517
Hong Kong (China)	0·390	0·387	0·493	0·620	0·785	0·886	0·915	0·915	0·842	0·650	0·493	0·405
Shanghai (China)	0·159	0·186	0·213	0·345	0·484	0·694	0·889	0·871	0·656	0·449	0·310	0·224

annual medical reports of Burma for evidence of cholera spreading eastwards from India. This is limited by the absence of any good road or railway communications between Assam and Burma, to the north by a mountainous area blocking the east end of the Brahmaputra valley, and to the south from the Chittagong district of Eastern Bengal by hilly country. Nevertheless a study of many annual medical reports of Burma reveals that some 300,000 labourers travel yearly to Lower Burma from Eastern Bengal, and they have been known to spread cholera during the spring rise in the incidence of the disease. Such outbreaks of cholera in Lower Burma should be controlled by the annual inoculation of such dangerous immigrants.

Moreover, although pilgrim traffic is on a much smaller scale in Burma than in India, there are a number of yearly festivals at the Burmese pagodas attended by some 280,000 pilgrims, who have frequently spread cholera outbreaks. They also should undergo compulsory inoculation every year, in view of the striking success of that measure in India in recent years.

Cholera Incidence and Meteorological Conditions

The data shown in fig. 2, which include material failures of the monsoon rains, must next be studied in the light of recent experience in India to ascertain whether epidemics of cholera in East Asia can be foreseen in time to allow of their being controlled by measures that proved effective in India.

The upper section of the chart reveals six years in which cholera epidemics of grade III spread over China from the south as far north as Manchuria. The first of these epidemics, in 1902, originated in the great Indian epidemic of 1900, which, as usual, followed widespread failures of the south-west monsoon rains in June to October of the previous year. The recorded deaths from cholera in 1900 in India were 797,273, or 3·72 per 1,000 of the population. This epidemic involved Burma in the same year; during 1901 and 1902 it spread eastward over Thailand and Indo-China, and was still prevalent in southernmost China in 1903. Hong Kong, the Straits Settlements, and the Philippine Islands were also involved.

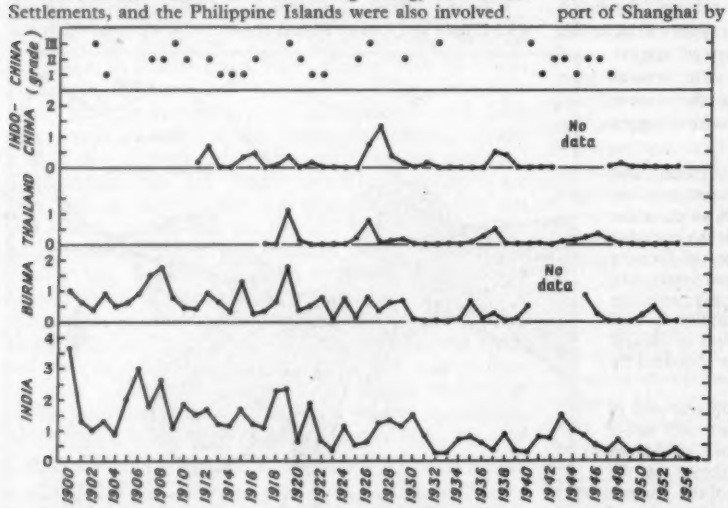

Fig. 2—Cholera deaths per 1000 population (India, Burma, Thailand, Indo-China) and grade of epidemics (China).

In the 1906–09 epidemic, India was involved in 1906–08, with cholera mortalities up to 1·43–1·68 per 1000, and China had grade-II outbreaks in 1907 and 1908, culminating in a grade-III one in 1909 extending as far north as Manchuria once more. Hong Kong, Singapore, and the Philippines were also involved. It is noteworthy that in China the 1907 summer monsoon rains were deficient—a shortage that almost always precedes cholera epidemics in India by resulting in scanty drinking-water supplies during the succeeding annual spring rise in cholera incidence.

In the 1918–20 cholera epidemic India showed the high cholera mortalities of 2·35 and 2·40 per 1000 in the first two years. Burma had the high rate of 1·53 in 1919 and Thailand one of 1·13 per 1000, the highest of the past half-century, with 10,277 deaths from cholera. In Indo-China the rate rose to 0·27 per 1000, and a grade-III epidemic once more spread north over China to reach Manchuria. It continued as a grade-II outbreak in central and south China in 1920, and as grade I for the next two years in south China only, with absolute humidities of January and February of almost 0·400.

The 1924–26 epidemic ran a very similar course to that of 1918–20, for the cholera death-rate rose in 1924 in both India and Burma and was followed by increased prevalence in Thailand in 1925 and 1926 and in Indo-China in 1926 and 1927, to reach the highest level in the series of years of 24,201 deaths, 1·34 per 1000, in 1927. This epidemic culminated in a grade-II epidemic in 1925 and a grade-III one in 1926, reaching as far north as Manchuria. It was again aggravated by a water shortage; the annual rainfall in Shanghai in 1925 was 13·85 in., or nearly a third of the normal.

In 1932 another grade-III epidemic affected China as far north as Manchuria, but was exceptional in not having been associated with high cholera prevalence in the countries to the south, except for a moderate rise of 1580 deaths, or 0·18 per 1000, in contiguous Indo-China. However, Wu Lien-Teh (1932) records that the first cholera death of this year was on the unusually early date of April 26, and the outbreak at Shanghai, near the mouth of the Yangtse, spread to the south and also north to Manchuria. The disease must have reached the great port of Shanghai by the coastal route from the south, as it has repeatedly been recorded to have done in the half-yearly reports of the medical officers at the Treaty Ports of 1870 to 1885, of which I have made notes. This serious epidemic involved 23 provinces and 212 large cities, but the actual number of deaths is not recorded. It was predisposed to by the low annual rainfall—a sixth below the average—and the occurrence of the first case as early as April indicates an early spring rise in the absolute humidity favourable to the early spread of the disease. These factors may account for the fact that there was an epidemic though Burma and Thailand had not shown any material increase of cholera in the previous year, as had preceded the previous grade-III Chinese epidemics already described.

In the case of 1940–47 China epidemics shown in fig. 2, few data are available because the second world war had involved both Burma and China. This period was accompanied

by high cholera-rates in Burma in 1940 and 1941 and in India in 1941–45. In India famine conditions followed greatly increased prices of food; famine-stricken crowds wandered over the country. The lack of data for the cholera deaths in the war years is illustrated by breaks in the curves in the chart.

The general conclusion is that cholera epidemics in China are essentially due to the spread of the disease from the endemic regions of Eastern Bengal, Burma, Thailand, and Indo-China (in years of increased prevalence of the disease) across the southern border of China over greater or less areas of that vast country.

Relation of Cholera Incidence in Burma to Meteorological Conditions

The incidence of cholera in Burma from 1877 to 1922, in relation more particularly to rainfall, is dealt with in my memoir (Rogers, 1928, pp. 156–162). It is there recorded that in every one of the fifteen years in which the cholera incidence was 50% or more above the yearly average, the rainfall during the preceding south-west monsoon of June to September, or during the succeeding October to December, or during both periods, was seriously in defect. Tables (Rogers, 1928, pp. 147, 149, and 151) show that the same relationship holds good in the adjacent endemic areas of Eastern Bengal and Assam. In all these areas the minimum cholera season is during the abundant rains of the south-west monsoon—e.g., in Lower Bengal only 4% of the total annual cholera mortality is recorded at this season. Exactly the opposite is the case in the epidemic areas to the north-west and west of Bengal, with absolute humidities below the critical point of 0·400 in the cold-weather months. As in the endemic areas of Lower Bengal and of Burma to Cochin-China, the absolute humidity during the cold-weather months never falls to the critical level. In these regions the annual rise in the cholera incidence starts in October to December, immediately after the cessation of the monsoon rains. Hence the early failure of the monsoon and of the rainfall of the last quarter of the year results in the early and continued rise of cholera incidence in October and November, with high total incidence in the twelve months from October onwards. Such years of high cholera incidence can thus be foreseen, though only very shortly before their occurrence. From the extensive endemic areas of Lower Bengal, Assam, and Burma to Cochin-China, the epidemics spread to the west of Bengal over the epidemic areas of India and from South-East Asia northward over China; but only with the rise of the absolute humidity to well above the critical point of 0·400 in March to May in India and from late April onwards in China, more particularly in the Central and Northern provinces. This allows ample time for large-scale preventive inoculations to be used to protect China from the spread of cholera from the endemic areas to the south.

Recent Cholera Incidence in India, South-East Asia, and China

The incidence of cholera has declined since 1947, with the exception of a rise in Burma in 1951 following deficient south-west monsoon rains. The great decline of the disease in India has been shown to be due to compulsory inoculations on a large scale, but this explanation does not apply to Burma, where the latest data from 1947 to 1956 show an average of only 202,000 annual anti-cholera inoculations—very small figures in proportion to the population, as compared with those in India during the same period. Moreover, the data show clearly that in years of low cholera incidence in Burma the inoculations fell to an average of under 50,000; this indicates that the inoculations were used extensively during outbreaks only when it was too late to control them.

On the other hand, recent years have shown an unusual number of good monsoon rains, unfavourable to enhanced cholera incidence, in both India and South-East Asia, which cannot be expected to continue much longer. Moreover, my studies of all the available Indian data from 1866, now extending over ninety years, show that very low cholera incidence in one year is liable to be followed by high rates whenever deficient monsoon rains favour a recrudescence of the disease; so preventive measures must be considered.

Control of Cholera in the Endemic Areas with the Prevention of Spread over China

All sanitarians will agree that the ultimate control of cholera depends on the provision of safe drinking-water to the million or so villages of India and probably still larger numbers in South-East Asia and China. The number of decades—or should it be centuries?—that will be needed for that purpose is anyone's guess. Meantime the authorities should consider the application to Far East Asia of the large-scale compulsory inoculation measures that have already met with success in India.

The principles of the new plan of control are simple, but their application will vary to some extent with local conditions. Thus in India the main task was the yearly inoculation of some twenty million pilgrims, who travel long distances through cholera-infected districts to attend religious festivals, become infected, and carry the disease back to their own villages. On the other hand, there is very little spread of cholera by coastal sea traffic, which is a feature of its extension into China from the south. All immigrants into China from the more southerly endemic areas should be inoculated against cholera at least a week before they are allowed to enter Chinese territories, preferably before embarking for the journey. In the case of ocean-going steamships, this is probably already provided for. Its great value is demonstrated by the long established inoculation of vast numbers of pilgrims to Mecca, which has put a stop to the spread of pandemics by them to South-East Europe, which were a feature of the 19th century. A more difficult problem is presented by the extensive movements by coastal traffic of small vessels and by the large boating population in the estuaries of the great rivers of China. Quarantine measures have for long been in use in Chinese ports, and judging from recent Indian experience, the advantages of regular large-scale anti-cholera inoculations are very soon realised by the people and have even led to their clamouring to be inoculated against cholera before undertaking journeys in cholera-infected areas. This should obtain still more if it also avoids quarantine measures, which are far more unpopular.

The appearance of cholera cases in vessels arriving in the more southern Chinese ports used to be a regular annual event, but the most serious epidemics have usually been due to overland spread in years of high cholera incidence in the endemic areas, as shown earlier. It is also on record that quarantine methods have always failed to avert such spread overland. The Chinese Government now have control of the northern portion of Indo-China; this will facilitate their control of the extension of cholera over southern China. But to avert the more serious

epidemic spread it will be necessary to keep a close watch on the development of high incidence of the disease in the cold-weather months, in Burma more especially, following deficient rainfalls during the preceding south-west monsoon and autumn period. This can now be done, owing to issue in recent years of the weekly bulletins of epidemic diseases by the World Health Organisation.

But to strike at the root of the problem it is essential that the endemic regions of Burma, Thailand, and Indo-China should adopt the successful Indian plan of enforcing compulsory inoculation every year of all pilgrims, immigrants, and other travellers from without and within their territories. This measure will require about a decade to bring about its full effects. But success should result, not only in the control of serious outbreaks in the territories concerned, but also in the prevention, in future years with extensive failures of the summer monsoon rains, of the pandemic spread of cholera over both Asia and Europe. One more scourge of humanity will then have been brought under control by medical science.

Conclusion

The incidence of cholera during the last half-century in the endemic regions of South-East Asia, and its epidemic extension northwards over China, have been studied. The adoption is advised in Far East Asia of the large-scale compulsory inoculations, which have already greatly reduced cholera mortality in India during the past decade.

I desire to acknowledge my great indebtedness to Sir Graham Sutton for supplying me with extensive meteorological data; to Dr. Wu Lien-Teh for the loan of his valuable papers on cholera in China, and to Dr. Charles Wilcocks and Mr. Cyril C. Barnard, both of the London School of Hygiene, for much help in obtaining literature on the subject.

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Points of View

MEDICAL PRACTICE IN A CHANGING SOCIETY*

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NEW problems and new solutions are continually arising in our society. Nothing is static. Medical practice influences social conditions, and these in turn affect medical practice.

Liberalism and Socialism

In the past half-century, side by side with the advances of science and their effects on our way of life, there have been two less tangible developments which have directed the policies of government and of all who have power to influence our thoughts, our ethics, and our morals. These are the acceptance of liberalism—using that word in its widest sense—and the partial acceptance of socialism.

By liberalism I understand the recognition of the value of the human personality—the belief that the individual human being should be free to exercise his peculiar abilities and energies, and that everybody has equal right to this freedom, regardless of social class or race. To put it shortly, liberalism insists on the brotherhood of man and is inspired by the Christian ethic. Not only has liberalism been accepted and cherished by this country, but it is generally accepted as the guiding principle of what we at present call Western culture. It is in no way a new principle, but it was not generally accepted fifty years ago. Today, though the best way and rate of implementing it is still a matter of debate, all three political parties in this country accept it without question. The educational reforms have been inspired by it ; the gradual narrowing of class distinctions is the result of it; and the gradual loss of the privileges of birth, and to some extent also of wealth, are the direct results of its acceptance.

In strong contrast to liberalism, with its insistence on the paramount importance of the individual, are the principles of socialism. These lay stress on the importance of the group, of the community, of the herd, and insist that the direction and control of our way of life should be in the hands of the community and ultimately of the State, the interest of the individual being secondary. The socialist idea has been partially accepted as essential for successful government in these times of intense economic competition between nations. Its progress is largely the outcome of the second world war when the best use of all our resources was a necessity, and centralised direction and control was the only means of coordinating effort. From these war experiences arise the almost obsessional clamour for planning, with the risk of totalitarianism and an oppressive bureaucracy.

Between the doctrines of liberalism and socialism this country continues to compromise with its traditional skill.

One present result is the Welfare State, with its National Health Service, retirement pensions, insurance against unemployment and accident, subsidised essential foodstuffs (especially for pregnant mothers, infants, and schoolchildren), free education, holidays with pay, legal assistance, housing subsidies, and so on. And to pay for all this we have crippling death duties, supertax, and a very high rate of income-tax especially on unearned incomes, which have removed any lingering vestiges of the feudal system and have almost abolished the landed aristocracy.

Science and Technology

The most obvious effects of science and technology on our standard of living and way of life come from the application of metallurgy and chemistry and electronics in the factory and in the home. But perhaps the greatest influence on our lives has been the development of what are generically termed communications—facilities for more rapid travel; the telegraph, telephone, wireless, and television; the cinema and the daily press. Through the printed or the spoken word, by visual demonstration, or by seeing for himself, each of us is kept closely informed of what is happening in any part of the world, and these events crowd on us daily or hourly. A person can no longer confine his interests to his immediate surroundings: no longer does his family and his work group provide him with all the incentives and reasons for his physical

* From a Pfizer postgraduate lecture to the Glasgow faculty of the College of General Practitioners.

and intellectual activities. Fifty years ago he was the member of a family and of a village community, or the citizen of a town; but now he is being gradually forced to see himself as a citizen of the world, who must share in the problems of his fellow men, no matter where they live or to what race they belong. The raw materials required in his work, essential for his continuous employment, may come from many countries and continents; and in order that the products of his work may be sold there must be not only a demand but also purchasing-power in countries that until recently he had never heard of. In the words of A. H. Compton, chancellor of Washington University in St. Louis :

> " One important change in our mode of life is that the contacts of person with person are becoming more frequent and more extensive. This growing interdependence is a part of the process of becoming more civilised. . . . At present we find ourselves becoming members of a world community. Thus the community to which one belongs is extending more and more widely until already in many of its aspects it embraces all of mankind." [1]

The influence on our way of life of these ethical and political principles and of the discoveries of science has been great, and is still active. The conditions are constantly changing and there is no sign of any slowing of the rate of change—no indication that we are nearing a stage of stability and security.

Changing Foundations of Medical Practice

Science and technology have affected the practice of medicine as much as they have affected social conditions. There have been great advances in preventive medicine, in diagnostic accuracy, and in therapeutics, and the general picture of practice has changed both for the family doctor and for the specialist.

More perhaps than any others, two advances are responsible for this change in the picture : one is the control of infections by means of the sulphonamide drugs and the antibiotics, and the other the increasing range of surgery, largely due to the dramatic improvements in anæsthesia. By control of infections and by successful surgery we can remove many of the basic causes of ill health or of death ; and this should, of course, always be our aim, though for most of our patients we still have to rely on the treatment of symptoms and any other aid we can offer while they recover their health and capacity, or fail to do so.

Besides the advances that enable us to remove the causes of ill health, there are others that help us to control abnormal processes or so modify the symptoms of disease that our patients can more readily recover, or at least continue in gainful occupation. In this category I need only mention the hypotensive drugs, the anticoagulants, the analgesics, hypnotics, sedatives, tranquillisers, and diuretics; and we look forward to the further development of treatment by synthetic hormones.

In diagnosis also, scientific advances have been impressive. The most important are the analyses of biochemical processes, in which the use of radioisotopes have proved a valuable tool. More obvious perhaps has been the development of radiodiagnosis to disclose the structural causes of disturbances of functions. The use of X rays and contrast media and of cardiac catheterisation allowing the clinician to define the lesions in diseases of the heart and circulation with the accuracy necessary for cardiac and vascular surgery, and similar developments in the diagnosis of diseases of the lungs and bronchi are essential to the increasing successes of thoracic surgery. Less dramatic perhaps, but no less intellectually satisfying are the advances being made by the hæmatologists.

The use of the scientific method has made the practice of medicine—preventive, diagnostic, and therapeutic—become more precise. For many of our patients we can now do much more to save or prolong their lives or to help them to live with their abnormality.

An analysis of clinical medicine stated by Wilfred Trotter some years ago is, I think, worth recalling at this time. He pointed out that clinical medicine includes an experimental science—a strictly scientific discipline—which requires that no conclusion be reached till the evidence is complete, but that for the most part the practice of medicine is composed of applied science, and a practical art. As I have indicated, the application of scientific discoveries to clinical medicine is a part of practice that is growing now at an increasing rate. But there remains the third constituent—the practical art by means of which we care for our individual patients, based on the experience of similar situations, on a cultivated intelligence, and on a knowledge of human beings. For its successful exercise, it requires sympathy with human suffering. It is founded on the personality and character of the practitioner and it cannot be taught, though it can be greatly encouraged by the example of teachers and senior colleagues. The same now as it was in the days of Hippocrates, this personal component of clinical medicine will be required in the future as in the past.

The Individual and the Changing Society

Much has been written of late years about the absence of real happiness, joy, and satisfaction among our people —in spite of the Welfare State, in spite of better physical health, in spite of all the labour-saving and increased leisure that applied science is giving us. From a variety of standpoints, the writers all agree that the situation is serious and that it results from the rapidity of the change in conditions of our society. They point out also that these changes and developments, in so far as they are the result of conscious design, are failing to produce the very benefits intended—namely, a fuller and a happier life for each individual.

Man is the most highly developed member of the animal kingdom and it is his nature to be continually seeking outlets for his endeavours; he cannot remain static, but feels an urge to progress and to develop the potentialities of his personality. For this he needs freedom. At the same time he is a social animal and can develop successfully and happily only in cooperation with other human beings, other personalities. He is assisted in this by the advances in science and technology which enable the life of each to become more closely identified with the life of mankind, but his ties to his family and to his local community have become looser.

At the beginning of this century the codes of behaviour acquired in the family circle and later at school and elsewhere were based on a long tradition, in which religion and pride of place in the community played considerable parts. People looked forward to a life in which these foundations gave stability; their futures were relatively secure, and their relations with their fellows followed a recognised pattern. Wider educational horizons have shaken the trust of the adolescent in the values and traditions of the family. It has been pointed out that the parent-child conflict is intensified during periods of accelerated change, and as Eisenstadt [2] puts it:

> " The transition from family to total society is necessarily fraught with severe emotional difficulties, as it necessitates redefinition and transformation of the individual's role expectations."

1. Compton, A. H. *Proc. roy. Instn G. B.* 1955, **35**, 788.

2. Eisenstadt, S. M. From Generation to Generation. London, 1956.

These emotional difficulties affect both the child and the parents.

Instead of receiving their moral, ethical and behaviour values from the family and the local community, adolescents, and adults also, now get them from many different sources—trade-unions, the Press, wireless, cinema, age-groups, clubs, the Army, and so on. These present a great variety of experiences from many countries with various cultural standards and competing values, many of which cancel out each other; and man lacks the psychological certainties of custom and precedent to guide and steady him.

In his *Diagnosis of our Time*, Karl Mannheim [3] says:

"We should not forget that moral codes, like legal regulations, are devices for moulding human behaviour. If we have so far been able to do without institutionalized control in the moral field, this is mainly because the ethical standards of everyday life have been created for the most part by trial and error, and transmitted by anonymous tradition. But trial and error only work as long as social conditions favour unconscious selection: that is, as long as changes take place so gradually that unworkable norms are sloughed away in the course of time. This is not what is happening today. The speed of transformation is surely too great to permit unconscious experiment and selection. The individual is lost in an invisible society, and is too weak to invent new norms for himself. The result is moral chaos in which religious standards, family traditions and neighbourly ethics are losing ground without being replaced by other principles."

and again:

"The most fruitful methodological device in science, namely to adjust if necessary our whole system of thought to the ever-broadening sphere of experience, becomes when applied to human life and moral issues, the greatest predicament of modern man. By developing the same kind of dynamic rationality in the moral world, modern man tends to lose a firm basis on which to stand. Whereas in some prominent individuals this falling into the abyss of the self without reaching the bottom presents itself as a grandiose struggle, in the average man the very same dynamics lead to a frivolous attitude of believing in nothing and to an endless craving for new sensations."

The average person, then, is suffering from the loss of the sense of security that arises in the absence of accepted standards of behaviour and of moral codes; but the changing social conditions are interfering also with the human urge to assert his individuality and to contribute his own peculiar talents in cooperation with his fellows. Even a partial acceptance of the principles of socialism induces uniformity. Man is moulded to a pattern by the education in the local-authority school, and in his work he must conform to the dictates of his union, the decisions of which he may have little, if any, say in determining. Service with the Armed Forces emphasises the same trend. The more the central planners are able to regulate our lives, the fewer are the opportunities of men and women to develop their talents and personality, and to progress.

Sir Alexander Gray [4] has expressed this concisely:

"... and Planning, as now understood, means among other things the removal from the decision of the individual or the electorate to the decision of the expert who is, by definition, always right"

and he concluded:

"I suggest to you, hesitatingly and for your consideration, that the Welfare State, in its unbounded benevolence, may find itself driven to a degree of regimentation and control which would make it in essence a government at least mildly totalitarian in character."

Though adoption of the principles of liberalism and socialism, and the advances of science and technology, are bringing enormous improvements in man's way of life and in the social conditions of this country, these are largely material and have been accompanied by a loss of stability and of the traditions that gave to each individual a sense of security. The average person feels frustration when hemmed in by regulations: he becomes restless and can find no outlet or relief. It becomes harder for him to cooperate with those with whom he is in contact in his work, and even in his home. These mental stresses so affect him that sooner or later his efficiency and his bodily health may suffer. Before long he seeks the help of his doctor.

The Changing Practice of Medicine

We saw how the advances of science have enabled us to be more precise and definite in the diagnosis of disease processes and to apply curative or corrective therapy to an increasing degree over a continually expanding field. It gives us intellectual satisfaction and professional confidence to be able to help those patients in whom the disturbance to health and well-being can be so dealt with. But perhaps we are, in consequence, less ready to spend our time and our energies on those patients whom we cannot help so directly, so dramatically. We may be tempted even to be less sympathetic towards them. It is disturbing to hear so often from members of the public "I didn't tell the doctor about that, he seemed too busy", or "I told the doctor, but he paid no attention to that."

It is well to take for granted that every patient who decides to visit a doctor feels fear or apprehension in some degree. Only rarely is it fear of death, but usually there is fear about inability to hold down a job, or to manage the household, or to look after the children, or perhaps merely to get the best out of life; and the mother's worry for a sick child can produce a strong and deep emotional upset. It is also a good rule in clinical medicine never to be satisfied with what has been done for a patient until the evidence is sufficient for a prognosis to be given, even if it would be unwise to state it. The prognosis is the answer to the question, often unspoken, "What does this mean to me?" or "What does this mean to my child?" Exclusion of organic disease does not in itself justify the diagnosis of a stress or psychogenic cause. If such a cause exists, the prognosis will depend on whether or not it can be eliminated or its effects modified, and for this to be possible it must be tracked down. No-one is more competent to do this than the family doctor with his previous knowledge of the patient, of the home, and of the other members of the family. Moreover, the therapy required for most of these patients needs no psychiatric specialist or expert training; common sense and a knowledge of the family and their environmental conditions are more valuable, and above all human sympathy and a desire to help and serve our fellow human beings—the essence of the practical art of medicine.

The obvious difficulty is, of course, that all this takes up precious time which the practitioner may feel would be better spent on patients suffering from more definite disease and for whom we can do something specific and up to date. But often more time can be found by better organisation of the work.

For example, P. M. Higgins [5] describes how the institution of an appointments system and a shift system for himself and his four partners eased the pressure on their time and accommodation. J. G. Ollerenshaw [6] shows how office work can be

3. Mannheim, K. Diagnosis of our Time. London, 1943.
4. Gray, A. *Univ. Edinb. J.* 1952, **16**, 146.
5. Higgins, P. M. *Lancet*, 1957, i, 680.
6. Ollerenshaw, J. G. *Med. World*, 1957, **86**, 251.

handed over to a receptionist and secretarial staff, and better use made of the services provided by the local health authority. Many practitioners, I think, are unaware of the help their local authority is prepared to give; and the more cooperation he establishes with the hospital service and his local authority the more time he will have to give to those patients whom he can best serve.

If the little enough time now available for leisure and recreation is not to be curtailed, clinicians should rid themselves of every task that can be performed as well, if not better, by others. In this way only can they meet successfully the challenge of a changing society. I must add that the most obvious means of getting more time to deal properly with the fears, apprehensions, and mental stresses of our patients is for each doctor to have fewer patients for whose care he is responsible, and this some doctors are doing.

Our profession has been accorded a peculiar privilege that distinguishes us from members of all other professional groups. This privilege has been given to us not by the State but by the people. They trust us and confide in us, and they ask us to relieve them of the burdens that unaided they find are too much for them. Because of this privilege, there is much more in the practice of medicine than the application of science. No matter how great the advances still to be made by the employment of the scientific method, there will always be a need for the practical art of medicine.

Conclusion

At present we are so busy preventing, diagnosing, and treating diseases that we have too little time left for treating our patients, for caring for them and relieving them of their burdens. But our patients are in greater need now than ever before of the care and devoted service that we have been especially selected and educated to give to them.

Medicine and the Law

Artificial Insemination not Adultery

CAN a wife who has borne a child as a result of artificial insemination be said to have committed adultery? This question came up for consideration recently in the Scottish Court of Session on the hearing of an action for divorce brought by the husband.[1] In a reserved judgment given last week, Lord Wheatley ruled that artificial insemination does not in law constitute adultery.[2]

The husband and wife had not lived together since March, 1954. In July, 1955, the wife gave birth to a girl. Her claim was that the child had been born as the result of artificial insemination through a donor, and that this was not adultery as the Law understood it. The husband maintained that he had never agreed to this course if in fact it ever took place, and that such a general defence was irrelevant.

Lord Wheatley, who described the case as unique in the annals of our Law, said that there were manifestly grave moral, ethical, social, and personal considerations involved in the practice of artificial insemination. It was almost trite to say that a married woman who was artificially inseminated in order to have a child who would not be the child of her marriage had committed a grave and heinous offence of contract of marriage; but the question for him to determine was not the moral culpability of such an act but whether it constituted adultery in its legal meaning.

His Lordship said that, having examined the Law of England on adultery and having found nothing to persuade him that the Law of Scotland was not the same on the subject, and having studied the opinions expressed by judges in other countries and in textbooks, he had reached the conclusion that artificial insemination did not come within the definition of sexual intercourse as understood by Scots Law. "Just as artificial insemination extracts procreation entirely from the nexus of human relationship in or outside marriage, so does extraction of the nexus of human relationship from the act of procreation remove artificial insemination from the classification of sexual intercourse . . . it follows that artificial insemination by a donor without the consent of the husband is not adultery as the Law interprets that term."

This judgment is not binding on the English courts, but it will undoubtedly have great persuasive value and is very likely to be followed if the matter ever comes up for consideration in England. Although the two legal systems differ in some important respects, there is a tendency for the courts of both countries to follow each other's decisions if possible. Lord Wheatley's view that there cannot be adultery without actual sexual intercourse is in line with English judgments on the nature of adultery. Thus manual gratification by a wife of another man's sexual organs has been held not to be adultery, although a breach of the obligations of marriage. The distinction between adultery (which is a ground for divorce) and various other breaches of the responsibilities of marriage (which are not necessarily a ground for divorce) is cardinal to the whole subject, and should not be overlooked in the debate which will no doubt result from Lord Wheatley's judgment.

1. *Times*, Dec. 6, 1957.
2. *ibid.* Jan. 11, 1958.

Public Health

Atomic Safety: a Report after Windscale

AFTER the accident at Windscale no. 1 pile last October, a committee, under the chairmanship of Sir Alexander Fleck, was asked "to review the organisation within the Authority as a whole for control of health and safety and to make recommendations." A summary follows of the committee's findings and recommendations.[1]

The accident revealed latent public anxiety about the risks of atomic-energy work. The precautions already applied were very elaborate; the aim must be to err on the side of caution. The accident revealed that the Authority's organisation was inadequate, but improvements in it must be supplemented by clarifying the relations between the many Government departments concerned with atomic safety, by coordinating the activities of these departments, and by building up the Atomic Energy Office to enable it to play the leading role. The measures needed for safety were formulation and observation of appropriate codes of practice, with numerical limits established by experiment and with monitoring of plant and operations by safety staff.

The hazards to be considered were exposure of workers to radiation, loss of control of a nuclear reactor (including unintentional assembly of critical masses), and discharge, as effluent or by accident, of radioactive matter.

The Authority's three groups (industrial, weapons, and research) should collaborate on problems of criticality, to ensure that a critical mass of material (i.e., that which leads to a nuclear reaction, giving rise to heat and fission products) was not assembled accidentally.

The committee agree with the Authority that an independent board should be set up to license nuclear reactors; but at present the only people competent for this were on the Authority's staff, and it must remain a long-term objective.

1. The Organisation for Control of Health and Safety in the United Kingdom Atomic Energy Authority. H.M. Stationery Office. Cmd. 342. Pp. 28. 1s. 3d.

Decentralisation of management in the Authority meant that health provision was not uniform. The report endorses the Authority's decision to set up a committee responsible for overall supervision of all matters of health and safety. The management of health and safety in the factories of the industrial group should be integrated into a single section responsible directly to the works general manager. The health and safety manager should be a physician of consultant calibre, with sound training in industrial health, special knowledge of the health aspects of radiological protection, and some knowledge of the associated problems in physics, chemistry, and engineering. If such a man could not be found, the best alternative would be a physicist with knowledge of the biological aspects.

One of the most important points emerging from the committee's review was the serious shortage of people with the necessary qualifications in medicine, radiology, health physics, and nuclear physics and engineering. Health and safety should be made an attractive career, with appropriate salaries and the provision of proper instruction. The Authority "should assume responsibility for building up the national supply of these health and safety specialists, who will be required in ever increasing numbers". The specialised training provided by the Authority should take eighteen months, full time, including up to nine months' study of radiation physics. The training should merit a new professional qualification. The Authority should also recruit and train, on the job, the new special works medical officers, and offer training to public and industrial health workers, sanitary and water engineers, and the police. This training should be carried out in a national centre, which would also cover the health and safety aspects of the use of istotopes in medicine, agriculture, and industry.

The Authority should review the procedure for the publication of information about accidents, and coordinate the site emergency procedures and bring them to a uniformly high standard in all units.

Londoners Last Year

A preliminary report on the health of the county of London in 1957 has been issued by Dr. J. A. Scott, the medical officer of health. The death-rate, at 11·2 per 1000, was the lowest (except for 1954) since 1948. Mortality was light in the mild first quarter, but there were 2000 more deaths than usual in the December quarter and the number of deaths from respiratory disease was twice the average. There were an estimated 350 cases of poliomyelitis, with 12 deaths. Tuberculosis mortality fell from 0·14 to 0·11 per 1000, and there were fewer notifications. 23,000 children were vaccinated with B.C.G.

The birth-rate rose, for the first time since the 1947 peak. Infant mortality was 0·35 per 1000 births—the lowest on record, except for 1956. 46% of pregnant women and 87% of children under a year attended the L.C.C. antenatal clinics.

The Third Quarter in England and Wales

The Registrar General has issued his report [1] for the quarter ending Sept. 30 last. His figures for births, deaths, stillbirths, and infant mortality confirm those given previously.[2] Other details include:

Population and life expectancy.—Abridged life tables are given, based on the mortality experience of 1954–56. The expectation of life in years for males (females in parentheses) is 67·6 (73·1) at birth, 68·6 (73·7) at 1 year, 50·3 (55·3) at 20, 31·4 (36·2) at 40, 15·0 (18·7) at 60, and 5·2 (6·2) at 80. Population tables show that males outnumber females in all age-groups up to 30; thereafter women outnumber men. The total population at June 30 was estimated at 45,043,000, including 2,070,000 men and 3,196,000 women aged 65 and over.

Infectious diseases.—The death-rate was 96 (91) per million from tuberculosis, 392 (267) from pneumonia, and 9 (3) from poliomyelitis (figures for third quarter of 1956 in parentheses). Smallpox caused 2 deaths, the first since 1953.

1. Registrar General's Quarterly Return for England and Wales: Third Quarter, 1957. H.M. Stationery Office, 1957. Pp. 24. 1s. 6d.
2. See *Lancet*, 1957, ii, 887.

In England Now

A Running Commentary by Peripatetic Correspondents

WITH some thousands of other citizens I spent last Wednesday evening "just messing about in boats". At Olympia there were hundreds of boats, large and small, round and flat, black and white, glass (yes glass) and wood; driven by air, oar, and diesel. They must have knocked the wall down to get some of them in, or else built them there: complex rigging soared skywards and was lost in the smoky haze around the second-floor gallery. At the other extreme sailing dinghies shrank to pram dinghies and canoes for achondroplasiacs: finally there was a sort of folding boat that could be carried in one hand like a bag. Doubtless there was an inflatable boat somewhere that fitted snugly into the vest pocket. Lifeboats, patrol-boats, and even the Armed Services were represented; one remarkable boat had rotors fitted with which the thing could fly in the air. But I didn't see a single raft. True there was a minute canoe about 8 in. across in which some madman crossed the Atlantic. But no rafts: shades of Kon Tiki and Jerome K. Jerome. Or maybe rafts are just a little bit *too* easy to make yourself in the back garden and not worth plugging. A splendid nautical atmosphere was created by the sounds of distant breakers and B.B.C. seagulls coming out of the diffusion system.

The clientèle looked rather dull: just like the people that go to the Radio Show, the Photographic Show, the Motor Show, and even our little Show. There must be a nucleus of people that attend all exhibitions for the heck of it without being especially interested: why of course there's me for a start. But the odd beard sprouting a curly pipe and covering a duffle coat suggested that some yachtsmen were present, and I heard one splendid salty character, a lifelong yachtsman to the tips of his bushy eyebrows, remark "Quite a good show all round—but too many d——d engines".

After an hour or two one gets a surfeit of seafaring: gallery after gallery of stoves, lamps, rudders, binnacles, and blocks stretch ahead. The salesmanship could learn a thing or two from our little show: nobody invited me to heave to and prepare to board, and I couldn't even cadge a sample tin of waterproof paint. So after taking on ballast at the canteen we luffed windwards to the exit feeling slightly seasick.

• • •

After the effects of turkey and cigar amblyopia had abated I settled down to analyse our Christmas-card series. 11% boasted holly, 11% Father Christmases (3 with reindeer and 3 using more modern means of transport—car, train, and sputnik). 10% showed a winter scene, but the orthodox seasonal balance was upset by 1 autumnal picture and 1 view of summer in Sydney (Australia). Food (mainly puddings with some of the 11% holly stuck into them) formed 7%. Coaches and carol-singers were surprisingly poorly represented (3% each) and robin redbreast was a melancholy single entry. Angels (3%—1% with tenor saxophone), flowers (4%), and simple unheraldic crests (4%) were significant. The most bizarre single entries are not included in the present series, but they included an etching of Frankfurt am Main, a blonde hanging up nylon underwear, and a photograph of a Nigerian woman fishing in the Limbe River. We shall have to wait till next year to see whether these are statistically significant.

• • •

One of the pleasantest English sports is catching trains. It is so democratic. And it has all the thrills of surprise and suspense. It induces such sympathetic participation in the spectators. Only the most antisocial refuse to enjoy the triumph of the train-catcher. Rarely, you get the exquisite sensation of watching an artist. How unruffled he is. How elegant and perfectly coordinated are all his movements as he darts through the barrier and springs lightly on to the moving train. You sink back into your seat with some of the afterglow that follows *Spectre de la Rose*.

As a warning to would-be emigrants to Canada I should like to quote from our railway by-law no. 99, approved by the Board of Transport Commissioners for Canada and sanctioned by His Excellency the Governor-General-in-Council:

> No person, except a servant or agent of the Company in the performance of his duty, shall open any vestibule door or stand upon the steps or platform of any car while it is in motion, or entrain on or detrain from, or attempt to entrain on or detrain from, any such car while it is in motion . . .

And in case anyone may think that a railway by-law means nothing, like no-smoking in English trains, they make it physically impossible to do what the by-law prohibits. Bars of steel lock all the doors before the train moves.

On board the train your safety is still the commissioners' main concern, even if you have villainously boarded the train without a ticket.

> Every passenger who refuses to pay his fare or produce and deliver up his ticket upon the request of the conductor, may, by the conductor of the train and the train servants of the Company, be expelled from and put out of the train with his luggage at any usual stopping-place; provided that the conductor shall first stop the train and use no unnecessary force.

The by-law that prevents you from leaping on to the moving train saves you from being flung off it, without your luggage, at some uninhabited spot. Too many romantic souls think of Canada as a wild, lawless, rough-riding, sharp-shooting territory. If train-catching is your sport, you'd better stick to the Euston Road.

* * *

In the West of England hospital where I was reared the loudspeaker caller system for members of the staff is unknown, and before I came to St. Euphonia's I had only come across it in American films.

It has various aspects that fascinate me. There is the Voice From Heaven impression. This feeling of being personally called to Judgment every few minutes wore off after a while. However, I still sometimes give an involuntary shudder when I hear my name called in a voice of doom, from outer space as it were.

The impression that has lasted, on the other hand, is that of being part of a cosmic game of Happy Families. "Calling Mr. Sparks, the Electrician", or "Calling Mrs. Potts, the Domestic Supervisor", never fail to put me in mind of the game I used to play as a child. It is a great pity that there is no way of reciprocating these demands over the loudspeaker. "Have you got Mr. Chips, the Carpenter?" "No, but have *you* got Mr. Wrench, the Engineer? *Thank* you; . . . *and* Mrs. Wrench, the Engineer's wife? *Thank* you."

After all, the normal working of the hospital could always carry on with coloured lights.

* * *

Last week one of our elderly patients, after an operation for an upper femoral fracture, showed evidence of basal lung congestion, and his sputum was sent to the laboratory for examination. The report came back: "The carton contained matchsticks." Orthopædic surgeons have gained many a nickname in the past fifty years—carpenters and monumental masons among them. Now I know why.

* * *

It's μ by name, but what by nature?
A line, you say? Diameter will do.
Erythrocytes are 7μ, God bless 'em,
Mm divided into 7 thousandth parts.
Cu μ is million millionth of a m(i)l
μl a litre's millionth is,
And μ of g, a thousandth milligramme.

Micron or microgramme, it's all the same,
A thousandth of a thousandth part. A μ!
Pass on the sign from lip to lip;
For don't expect to find, my son,
This measure μ defined in books. Eheu.

Letters to the Editor

SURGERY OR RADIUM FOR CANCER?

SIR,—It is with regret that we notice that Professor McLaren and his colleagues (Jan. 11) are using our recent communication as an occasion for reopening the old battle between radiotherapy and surgery in the treatment of cancer. This battle may have been necessary once, but there can be little doubt that radiotherapy has become established as a therapeutic agent of immense value. Today, therefore, there should be no prejudice or partisanship in the treatment of cancer—particularly carcinoma of the cervix, where it is of vital importance to the patient not to fall into the hands of either a surgical or radiation enthusiast, since each will use the method he knows best, and this may by no means coincide with the patient's best interest. One of the main functions of the joint clinic, the work of which has been reported, is to safeguard the patient against the risk of such misguided enthusiasm and ensure that she receive the most appropriate treatment, whether surgical or radiation, under the best conditions.

Our object in reporting the work of the joint clinic was:

(1) To show that surgeon and radiotherapist can work in harmony as a team under ordinary hospital conditions.
(2) To give some idea of the usefulness of such a clinic as reflected by numbers and types of case referred to it.
(3) To determine the advantages, if any, to the patient of the cooperative services thus made available.

To this end we compared the methods used and the results of treatment before and after 1944.

It was not our aim or purpose to "do justice to surgery" or to "mention modern surgical results." There is already a wide literature on these themes and we would specially commend to Professor McLaren and his colleagues' attention Kottmeier's [1] analysis of surgical and radiation results, in which he shows convincingly that, with comparable clinical material, radiotherapy gives results equal to those claimed for surgery by Meigs and others. Because we were conscious of our poor results in stage I (60·4% at 5 years), we undertook the "manœuvres" commented on by Professor McLaren—not, as he claims, to boost our radiotherapy cures to the detriment of surgery, but rather to boost our own morale. It is always a cause for humiliation and self-searching if one's results are worse than those claimed by other workers. The purpose of the discussion quoted by Professor McLaren was to show that under other and more fortunate conditions we, too, might have attained the 70% 5-year survival rates achieved by other workers which would have substantiated more firmly our statement that "It therefore seems that radiotherapy is not only undoubtedly the correct treatment in inoperable cases, but also usually the preferable treatment for operable cases." This statement forms the substance and flesh to be found on the seasonable but scrawny bird mentioned by Professor McLaren. Our statistical turkey was both home plucked and killed, since all the statistical tables were drawn up by one of us (C. A. S.) in the hope that our conclusions would not be befogged by the use of a multiplicity of incomprehensible statistical terms, usually much in evidence when unpalatable facts have to be obscured.

We would summarise by repeating that our opinion based on our experience since 1944 is that in our hospital the results in stage-I cases (60·4%) submitted to radiation treatment compare well with those obtained when the Wertheim operation is performed (65·1%). In these circumstances we customarily recommend radiotherapy to our patients with carcinoma of the cervix (with the exceptions listed in our paper). To be able with confidence

1. Kottmeier, H. L. *J. Obstet. Gynæc., Brit. Emp.* 1955, **62**, 737.

to offer a patient the opportunity of avoiding a major mutilating operation, we regard both as a gesture in the best tradition of medicine and as a happy reward for our labours over the past years.

J. B. BLAIKLEY
M. LEDERMAN
C. A. SIMMONS.

Chelsea Hospital for Women, London, S.W.3.

A DISTRICT MENTAL HEALTH SERVICE

SIR,—The Worthing Experiment, with an outpatient and domiciliary psychiatric service, described in your issue of Jan. 4, is so obviously a step in the right direction that its success was assured. We are particularly interested in the extensive use made of outpatient electroconvulsant therapy, since, for many years, we have regarded this procedure as the only method of substantially reducing the need for mental-hospital admissions.

The Sheffield Mental Hospital, with its 2089 beds, has, since the last war, been responsible for a catchment-area population of a million people—a ratio of 2 beds per 1000, compared with 3–5 per 1000 for the country as a whole. Admissions have of necessity been restricted to severely disturbed patients for whom outpatient treatment is inadvisable. But it was fortunate that in 1942 outpatient electroconvulsant therapy first became practicable, and since then, the Sheffield Hospital has maintained an active unit which, in recent years, has provided up to 1000 treatments a year with satisfactory results in the moderately severe case of depression which could not be admitted because of shortage of beds. A special treatment-session is reserved for geriatric patients.

If it is estimated that the gross incidence of psychosis in the community is 9 per 1000, or 1800 cases in a 200,000 population, not more than a third of these will probably require inpatient treatment and not all in the same year.

We therefore applaud the results achieved by Dr. Carse and his colleagues, which amply support their plea for expansion of outpatient facilities in psychiatry. It would seem that a unit of the Worthing type should be provided for each 200,000 population, and, until an effective substitute for modified electroconvulsant therapy can be found, each unit should be able to provide 30 to 40 treatments per week.

F. T. THORPE.

Middlewood Hospital, Sheffield.

SIR,—I have read with interest the report by Dr. Carse and his colleagues on the Worthing experiment for a similar service has been in existence in most parts of the Manchester region for several years and its value is well recognised.

In Bolton, for instance, a small psychiatric unit at a general hospital provides diagnostic and treatment clinics, day-hospital facilities, domiciliary service, and a psychiatric social club run jointly with the medical officer of health.

Under present legislation, however, the success of a district service must depend on the cooperation of the local health authority and the support of the regional mental hospitals. In Worthing the full cooperation of Graylingwell has apparently been enlisted, but it would be of interest to know how the public-health services have fitted into the scheme and what part the D.A.O.s. play. The high degree of screening before admission to Graylingwell is certainly impressive.

In some areas of our region it is felt that unless the local authority can provide more welfare and hostel accommodation the work of district mental health service will be hindered. It is also important that a clear division should exist between the functions of a local psychiatric service and that of a large mental hospital. With early outpatient treatment mental hospital beds will be needed mainly for the more severely disturbed and long-standing patients, many of them aged, and some hospitals—overcrowded as they are—may be reluctant to accept these "less promising" patients. On the other hand, our experience shows that if a local service is accepted by the community, many patients are less willing to enter large mental hospitals.

Finally, a clear system of priorities should be drawn up. Once the facilities are available there is a constant increasing demand for the service, and the treatment centre may soon turn into a disposal centre for the increasing number of geriatric, "chronic sick" patients, not to mention additional work, brought by such agencies as the courts, probation service, and children's officers. Unless the service is as well staffed as Worthing's seems to be, delays and disappointments will be inevitable.

J. T. LEYBERG.

Royal Infirmary, Bolton.

ANTIBIOTIC PROPHYLAXIS

SIR,—In reference to your valuable annotation (Jan. 4), I should like to express my full agreement with your conclusion that antibiotics should not be used to prevent sepsis. One risk is that of sensitisation. This occasionally follows the prophylactic use of penicillin. The result is disastrous if the antibiotic has, at any time later, to be used to combat actual sepsis.

When arthritis is caused or aggravated by focal sepsis, the eradication of the focus may be essential to cure. Here prophylaxis of some kind is necessary to prevent what otherwise might be a severe reaction. Over many years I have never found prophylaxis with one of the sulphonamides to fail. I have always prescribed sulphathiazole 1 g. 4-hourly for 24 hours before and 48 hours after the operation. Now that long-acting sulphonamides are available, 1 g. daily for the same period has so far worked equally well.

H. WARREN CROWE.

London, W.1.

COMBINED BARIUM MEAL AND CHOLECYSTOGRAPHY

SIR,—Dr. Robinson [1] evidently does not favour any technical variation which might interfere with the accuracy of cholecystography, but perhaps he expects too much from this examination. There are claims that cholecystography is 96–98% accurate. The confirmation of the radiological findings is based on surgery, which by inference must limit the criteria for pathology to non-function or the presence of gallstones. Where cholecystography fails is in chronic cholecystitis in a gallbladder which still retains some function. It might seem possible to assess function according to the density of the shadow, but there are so many factors—physiological and physical—which influence contrast that such an examination would be almost valueless. When the demands of a large general hospital can be eased by a combination of examinations it is reasonable to adopt this technique, and we cannot agree with Dr. Robinson that the fine detail of the examination is sacrificed. Indeed we have made some striking films of small calculi.

In reply to Mr. Forty,[2] we certainly agree that calculi may exist without producing symptoms, but this also applies to a non-functioning gallbladder. It is in these patients that the combined technique is so useful in bringing to light associated lesions in the gastrointestinal tract which may account for some of the 30% of postoperative failures discussed by Ogilvie.

In a recent series of 2000 patients examined by this combined technique, 193 (9·7%) had pathological gallbladders. 100 of

1. Robinson, M. I. *Lancet*, 1957, ii, 1170.
2. Forty, F. *ibid.* p. 1339.

these showed no evidence of function, and 93 functioned but contained opaque or non-opaque calculi.

	Functioning with calculi	*No function*
Normal barium series	54	61
Duodenal ulceration	6	6
Gastric ulcer	2	4
Radiological evidence of gastritis	0	1
Hiatus hernia	11	10
Carcinoma of stomach	1	0
Duodenal diverticula	4	5
Previous gastrointestinal operations	9	5
Two or more of the above lesions	3	4
Miscellaneous	3	4

In a total of 193 pathological gallbladders, 78 had an associated lesion in the upper alimentary tract.

Department of Radiodiagnosis, University of Leeds.

A. S. JOHNSTONE
M. D. SUMERLING.

MANIPULATION FOR BACKACHE

SIR,—As Mr. Bremner (Jan. 4) infers, a great deal of nonsense is talked about manipulation. It is therefore a pity that his painstaking work is invalidated by the complete absence of control cases in his series. When dealing with something as personal as low-back pain it is impossible to eschew patients' subjective impressions, but I find it difficult to believe that so few of his cases exhibited abnormal physical signs. Thus instead of a useful statistical stick with which pro- or anti-manipulation extremists might have been beaten; we are left with just one more straw composed of clinical impressions.

One must also deprecate Mr. Bremner's failure accurately to define on *clinical* grounds what is meant by "lumbosacral strain". Even when accompanied by a half-hearted apology, usage is no excuse for the use of such a term which, though certainly "concise", is meaningless as he himself demonstrates. This does nothing to further the introduction of order into the chaos of dogma and empiricism which surrounds the subject of backache and its treatment.

Finally, it should not prove very difficult to explain the incidence of backache in the ratio of 1·8 females to 1 male in Mr. Bremner's series. A careful analysis of how the average day is spent would probably show that most of the 116 married women were subjected to more "externally applied strain" than most of the 84 males. The average modern housewife does not apply many sudden, violent, and dramatic strains to her back, but the sum of the stresses imposed by household chores, children, and not infrequently a whole- or part-time job as well, is immense, as can be testified by any husband who has tried to cope alone for a few days.

St. Thomas Hospital, London, S.E.1.

D. R. L. NEWTON.

SIR,—Being "osteopathically" inclined, and seeing many patients with backache, I was interested and pleased to read Mr. Bremner's article (Jan. 4). I should like to point out that we osteopathically inclined have never claimed a 100% cure-rate, but we do claim a high proportion of good results. I was particularly pleased to see such good results even with non-specific "orthopædic" manipulation.

If we use greater care in diagnosis instead of grouping all patients together under this vague heading of "lumbosacral strain", and if specific treatment is given to each type of low backache, then the results should be still better than those quoted by Mr. Bremner. This is in fact so.

If we lumped together all patients with indigestion and treated them with alkaline powders, there would be some good results; but if they were analysed carefully and treatment prescribed accordingly, there would certainly be a higher percentage of good results.

Differential diagnosis of low backache is difficult, but it is a mistake to say that "physical signs are few or absent". The points to look for are: the mobility range of both the area and the individual joints; the tenderness in interspinous ligaments; the tension in the erector spinæ muscles; the relative position of one vertebra to the next; the kyphoses, lordoses, and scolioses; and finally changes in the erect radiographs and mobility films.

The first and fundamental differential point is to distinguish between hypermobility and hypomobility. To manipulate joints which are already hypermobile is likely to give bad results. The differentiation can be made by palpation and mobility radiographs.

If there is hypomobility but no lesion or root signs, manipulation is almost always indicated. The next point is to locate the site of restriction so that the manipulation can be applied to the faulty joint rather than to the whole lumbar spine. It is better, and easier, to achieve a specific manipulation without an anæsthetic than with one.

If hypermobility is found, a corset and strengthening exercises are indicated, or injections of sclerosing fluid into the interspinous ligaments.[1]

Mr. Bremner found that in 3·6% of patients the condition was aggravated by manipulation. These, and some of those not improved, probably had the hypermobility type of low backache where the ligaments are overstretched already. I realise that his series aimed specifically at determining the benefit or otherwise of one manipulation, and to that end the experiment is to be commended. But if in private practice one were to make 3·6% of one's patients worse, it would soon ruin the practice. A bad reputation travels faster than a good reputation.

London, W.1. ALAN STODDARD.

SEX REVERSAL

SIR,—Dr. Ashley and Dr. Jones (Jan. 11) are to be congratulated on their critical discussion, which helps to clarify the position of their lucidly presented case in the increasing complexity of intersex states. I have recently seen three unusual examples of gonadal dysgenesis, all with male nuclear sex.

The first patient, an otherwise classical example of Turner's syndrome with short stature and webbing of the neck, has apparently menstruated for seven years; the second is a colour-blind dwarf whose father has normal colour-vision, and the third is a tall eunuchoid female with no stigmata of Turner's syndrome. The third case, similar to those reported by Swyer,[2] and different from that of Ashley and Jones in that the leucocytes show typical male morphology, is probably a variant of gonadal dysgenesis,[3,4] and helps to stress that reclassification is required.

You rightly say, Sir, that there is urgent need for a new terminology, and though your discussion is mainly concerned with examples of sex reversal, it is very important that any classification must also include cases of chromatin-positive Turner's syndrome and of chromatin-negative Klinefelter's syndrome. At the symposium on nuclear sex, a committee was appointed to consider the question of nomenclature, but your plea of urgency suggests that the matter might now be discussed profitably in your columns.

In the many types of pseudohermaphroditism, which include testicular feminisation and congenital adrenal virilism, gonadal sex and nuclear sex are in confirmity and the defect is apparently not primarily due to dysgenetic gonadal development. In other intersex states, however, gonadal involvement does appear to be of primary importance and the corticomedullary balance theory of gonadal differentiation seems to be a suitable basis for classification and nomenclature. Such a scheme, which can be conveniently tabulated and is self-explanatory, is offered below for comment. Some of the least ambiguous of the old names, shown in parentheses,

1. Hackett, G. S. Joint Ligament Relaxation. Springfield, Ill., 1956.
2. Swyer, G. I. M. *Brit. med. J.* 1955, ii, 709.
3. Hoffenberg, H., Jackson, W. P. U. *ibid.* 1957, i, 1281.
4. Swyer, G. I. M. *ibid.* p. 1421.

might continue to be used; but a name is required for the case recorded by Ashley and Jones, and a new name for the Klinefelter syndrome and its modifications is long overdue.

CLASSIFICATION AND NOMENCLATURE OF INTERSEX STATES

I. Both Gonadal Components Dysgenetic

(1) Underdevelopment:
  (*a*) Complete failure: Corticomedullary agenesis (gonadal agenesis).
  (*b*) Partial failure: Hypoplastic corticomedullary dysgenesis (gonadal dysgenesis).
(2) Overdevelopment of the component which should have been suppressed with collateral development of the other components: Hyperplastic corticomedullary dysgenesis (true hermaphroditism).

II. One Gonadal Component Dysgenetic (with non-development or suppression of the other component)

A. *Gonadal medulla dysgenetic*
  1. Overdevelopment: Hyperplastic medullary dysgenesis. (Chromatin-positive Klinefelter's syndrome.)
  2. Underdevelopment: Hypoplastic medullary dysgenesis. (Chromatin-negative Klinefelter's syndrome.)

B. *Gonadal cortex dysgenetic*
  1. Overdevelopment: Hyperplastic cortical dysgenesis (case of Ashley and Jones).
  2. Underdevelopment: Hypoplastic cortical dysgenesis (recognition awaited, but perhaps the case described by Hoffenberg et al.[5] would fit).

Glasgow. JOHN S. S. STEWART.

GALLSTONES AND THE SURGEON

SIR,—In your leading article of Dec. 21 no mention is made of intraoperative cholangiography. The indications for exploration of the common duct given by Ogilvie [6] are rather vague, and in fact they may be misleading. In the majority of cases intraoperative cholangiography reveals unequivocally the presence of stones or papillitis.

Department of Surgery,
University Hospital,
Basle, Switzerland. RUDOLF NISSEN.

A THYROID ASSOCIATION

SIR,—The suggestion from Professor Fraser and his colleagues (Jan. 11) for forming a Thyroid Association of Great Britain deserves the very strong and full support of all those interested in thyroid disease.

Such an association could be greatly strengthened by extending membership to Ireland and the Commonwealth, where valuable scientific contributions are continually being made.

A similar association in Europe would then work in close harmony with this body and the well-established American Goiter Association and their related endocrine societies.

Regional advance in the understanding of thyroid and allied diseases could be stimulated and canalised by each of these bodies and periodically coordinated by more frequent international meetings.

No international goitre meeting has been held previously in Great Britain. The last such gathering took place in Washington in 1938. With to-day's easy and rapid air travel, these long intervals seem out of date in such a swiftly advancing field of research.

As I said in your columns [7] and elsewhere [8] in advocating an international meeting on thyroid nomenclature, much potentially valuable work is being invalidated by uncoordinated methods of investigation and procedure. This is particularly so where advances in thyroid research have recently invaded so many fields and disciplines.

The flourishing American Goiter Association, at whose meetings we have been made most welcome, is an example of the great good such a body can achieve. The invaluable active support of the Royal Colleges of Surgeons and Physicians would also give a strong impetus to the creation and growth of a similar organisation in our midst.

London, W.1. T. LEVITT.

5. Hoffenberg, H., Jackson, W. P. U., Muller, W. H. *J. clin. Endocrin.* 1957, **17**, 902.
6. Ogilvie, W. H. *Ann. R. Coll. Surg. Engl.* 1957, **21**, 319.
7. Levitt, T. *Lancet*, 1957, ii, 1065.
8. Levitt, T. *Postgrad. med. J.* 1957, **33**, 352.

RADIATION AND LEUKÆMIA

SIR,—The data reported in our study of leukæmia in patients irradiated for ankylosing spondylitis (to which Dr. Pochin refers in his letter of Jan. 4) were collected at the request of the Medical Research Council, in the hope that they would provide some indication of the nature of the relationship between the dose of radiation and the resulting incidence of the disease. Although it was realised that no direct information would be obtained about the effect of doses as low as those commonly given in diagnostic radiology, it was hoped that it might be possible to estimate their effect by extrapolation from the results at higher levels of dose. It transpired, however, that quite a large number of patients were given radiation to areas other than the spine and sacroiliac joints, and for these patients it proved impracticable to estimate the size of the relevant dose (assumed to be the mean dose to the active bone-marrow). Our principal analysis was, therefore, limited to the group of patients whose treatment was directed solely to the spinal axis and for whom we obtained reasonably accurate data on the distribution of radiation dose within the spinal marrow.

In this group 18 patients developed leukæmia. The mean spinal-marrow dose received by these patients varied between 315r and 2195r, and it is clear that the data could not provide firm evidence of the quantitative effects at really low levels of dose. On the other hand, the data gave no positive indication of the existence of a threshold below which no effect was produced, and the incidence of leukæmia observed in the general population (presumed to have had no therapeutic dose) was close to that estimated for zero dose from the observed incidence at other levels. We therefore suggested, as a working hypothesis, that there was no threshold dose for the induction of the disease and included the point representing the estimated incidence for zero dose in the data from which the quantitative relationship between dose and incidence was calculated.

If (as Dr. Pochin suggests) the point for zero dose is omitted, and a regression line calculated from the incidence-rates for spondylitic patients alone (standardised for age and weighted according to their reliability) we obtain the equation $y = 0{\cdot}00634x - 0{\cdot}34$, where y is the annual incidence per 10,000 men at risk, and x is the mean spiral-marrow dose in röntgens. Hence the estimate of therapeutic dose which would correspond to zero incidence is 54r.

In view of the paucity of data the error of this estimate is liable to be very large. If the probable limits of the regression line are calculated by a method similar to that derived by Irwin,[1] it is found that the 95% confidence limits for the "true value" of the dose corresponding to zero incidence are −1700r and +400r. In other words, the threshold value may be zero or anywhere between zero and 400r. This calculation is made on the assumption that all the cases of leukæmia in the treated series were due to irradiation. If, however, some of the cases were due to other causes, the estimate of the probable threshold dose would be slightly higher. If no case of leukæmia occurring in the general population was due to irradiation, the estimated threshold dose would correspond to an incidence in a sample of the general population of the same age-distribution as that in the population of spondylitics (i.e., 0·49 cases annually per 10,000 men) and would be about 130r therapeutic dose with a likely upper limit of about 460r.

All these doses, it must be stressed, are mean doses to the spinal marrow. If it is assumed that there is a linear relationship between dose and incidence and that there is no threshold for the induction of the disease, it is possible to convert a mean spinal dose into a mean dose to the whole active marrow. In our report this was done by dividing by a factor of 2 to 3, since it was thought that

1. Irwin, J. O. *J. Hyg., Camb.* 1943, **43**, 121.

the spinal marrow constituted between a half and a third of the total active marrow. If, however, it is postulated that a threshold exists, such a conversion is impossible; in this case, there is no real justification for using a mean spinal dose as the measure of effective dose in the study of the dose/response relationship, and it might be thought preferable to relate the incidence of leukæmia to the maximum dose received at a point in the marrow. Such an analysis was made during the course of our investigations, and the results were reported in Appendix B of the Medical Research Council's report on *The Hazards to Man of Nuclear and Allied Radiations*. This analysis also provided estimates of incidence which appeared to be proportional to the dose and certainly gave no indication of the existence of a threshold. For reasons which are discussed in our report, however, we felt that this method of analysis might introduce a systematic bias into the results, and we preferred to use the mean spinal marrow dose as the best estimate of the effective dose.

In conclusion it is clear that we continue to be ignorant of whether or not a threshold dose exists. One way in which the problem may be solved is by undertaking further epidemiological studies, comparable to the survey of irradiated cases of ankylosing spondylitis. To plan such surveys, however, it is necessary to proceed on the basis of some hypothesis. The data obtained in our study led us to the conclusion that the most reasonable hypothesis to work with was that no threshold existed and we see no reason to modify it. We hope that no-one will mistake the delineation of a working hypothesis for a statement of established fact.

M.R.C. Group for Research into the General Effects of Radiation, Radiotherapy Institute, Western General Hospital, Edinburgh.

W. M. COURT BROWN
RICHARD DOLL.

A THEORY OF NERVE DEAFNESS

SIR,—The hypothesis of Mr. Gregory and Miss Wallace (Jan. 11) concerning causes of impairment of hearing in what they call " nerve " deafness is interesting, but it seems to me that they formulated this view with only limited background information about the various types of non-conductive impairment of hearing.

They mention that the terminology of non-conductive deafness is confusing, but surprisingly they themselves made a mistake leading to further confusion. They call an impairment involving predominantly high frequencies " presbyacusia ". This is, however, a term used for one definite type of deafness, clinically well known—that is, old-age deafness. Old-age deafness has some distinct peculiarities, and therefore to call all types of high-note impairment by this term is confusing. Moreover, they call this type of " nerve " deafness, characterised by a predominantly high-note loss, the typical one, and imply that it is numerically the most important, allowing certain generalisations. This is incorrect. There are several types of deafness (not conductive) which do not have this " typical " predominantly high-frequency loss. Even in Ménière's disease, in the more developed cases, the audiogram is more often " flat "—that is, showing a more or less uniform loss for all frequencies. Another type of non-conductive deafness in which the lesion is also in the end-organ (that is, deafness from maternal rubella) has also this characteristic " flat " audiogram without a predominantly high-note loss. There are some indications of recruitment also in these cases of deafness from maternal rubella.

Further, there are types of hearing loss, undoubtedly non-conductive, in which not only is there no predominantly high-note loss, but the hearing is distinctly *better* for the high notes. We are at present studying these types, and I have not only numerous audiometric records available but also *histological* evidence that the lesion is undoubtedly in the end organ—namely, in the organ of Corti.

In all these cases, of course, there is a considerable reduction in channel capacity of the communication system, caused by some disturbance in the end-organ, but no reduction of high-note discrimination as a result of it. This is against the suggestion of Mr. Gregory and Miss Wallace that reduction in channel capacity by an end-organ lesion leads to an impairment of high-frequency discrimination.

I must also mention that not only is there often a tendency in " nerve " deafness for an inner-ear lesion to produce a uniform loss for all frequencies but also a typical predominantly high-frequency type of deafness is often caused by a lesion which is *not* in the end-organ but higher up in the auditory pathway. A good example is deafness from hæmolytic disease of the newborn. We are studying another type in which there is also a symmetrical loss predominantly for the higher frequencies, and in which we have good reasons to believe that the location of the damage is not in the end-organ but at certain levels in the auditory pathway. We hope to report these findings soon, and also to give a theoretical explanation why the high frequencies are affected.

I am not saying this to dispute the possibility that, in some cases, random neural noise, affecting unfavourably the noise-to-signal ratio, may not impair discrimination in the high-frequency range; but when a general hypothesis is formulated at this early stage of study, it is dangerous to disregard certain factors which contradict it from the beginning. This may lead to a false theory.

Audiology Unit,
Institute of Laryngology and Otology,
London, W.C.1.

L. FISCH.

LABORATORY DIAGNOSIS OF CONGENITAL GALACTOSÆMIA AT BIRTH

SIR,—In the article by Dr. Schwarz and his colleagues describing the laboratory diagnosis of congenital galactosæmia at birth (Jan. 4), reference is made to a milk-free diet described by Holzel in 1954.[1] In his original article Holzel states this diet to be ". . . a modification of Moll's pudding, consisting of Farex, eggs and sugar in appropriate dilutions . . ."

May I draw your attention to the fact that the present preparation of ' Farex ' (Glaxo) contains separated milk powder? This has been added to the product since September, 1954, so that farex now contains 5% separated milk powder and 2·5% lactose. In view of the varying tolerance to lactose exhibited in those cases of galactosæmia reported in the literature, it seems advisable that those who may need to use farex should be made aware of its present composition.

St. Bartholomew's Hospital,
London, E.C.1.

MARY FURNIVALL
Chief Dietitian.

PREGNANCY AND COARCTATION OF THE AORTA

SIR,—I have read with interest the article by Dr. Goodwin (Jan. 4) on the risks of pregnancy in coarctation of the aorta, in which he analyses 13 cases of his own and 123 cases previously published. He concludes that the hazards of pregnancy in unrelieved coarctation depend largely on the presence or absence of added cardiovascular lesions, especially those of the aortic valve. As prophylactic resection of the coarctation is being increasingly performed in young persons, the prognosis of coarctation treated conservatively will become harder to assess. I wish therefore to report a case seen in general practice.

1. Holzel, A. *Med. ill.* 1954, **8**, 44.

A woman, aged 37, has coarctation and pulmonary tuberculosis. When she was 19, she was referred to a tuberculosis officer for his opinion, and coarctation was first diagnosed by the radiologist from the well-marked notches on the ribs. Full assessment at that time showed no hypertension (blood-pressure in arms 130/80 mm. Hg), and no evidence of aortic incompetence or other cardiac lesion. The electrocardiogram was normal. Subsequently she married, and had four normal pregnancies terminating in one forceps and three normal deliveries. Her last pregnancy was at the age of 35, and she was sterilised during the puerperium. Although her blood-pressure has been labile, she did not develop hypertension during any of her pregnancies, and only during the past year has her blood-pressure started to rise. Her coarctation remains remarkably symptom-free, and she leads the full life of a busy housewife. She has moderate dyspnœa on exertion, which is largely a sequel of pulmonary tuberculosis.

This patient's history confirms the fact that careful conservative management of four pregnancies may be undertaken without deleterious effect when coarctation is uncomplicated by additional cardiac disease.

Bungay, Suffolk. W. M. JORDAN.

A FUNCTIONAL NECESSITY

SIR,—I was much interested by Professor Platt's letter [1] on the subject of consultant appointments, and I heartily agree with him that it would be wrong to create a new subconsultant grade. However, a prerequisite to proper staffing is a knowledge of the needs of the individual regions, and such knowledge seems peculiarly hard to acquire.

When I was a member of the North West Metropolitan Regional Hospital Board's medical committee, it took me some months to get the officials even to allow a discussion on this subject. When we asked for the report of the Ministry of Health working party which had reviewed the consultant establishments of the region, we were informed that their report had never been published. In September of last year I once again endeavoured to ventilate this subject in the medical committee of the board. A request for details of the existing consultant and S.H.M.O. establishment in the region, and for information about all requests for additional consultant appointments, was met with the written reply:

"The information requested would be most difficult to assemble and would involve a close examination of all the Board's records on medical staffing since 1948. . . . Quite apart from this the Board's staff is so sorely pressed at the present time that to embark on this project would be quite impossible".

When regional-board officials and others show such scant interest in a problem of major importance, and when serious impediments are placed in the way of medical committee members who endeavour to secure factual information, it would seem high time for the Joint Consultants Committee to urge a nation-wide review of consultant establishments. I would further suggest that the various regional consultant and specialist committees should press their respective regional boards so as to ensure that the necessary information is made available. Once our professional committees have the facts it may be easier to overcome the deadly inertia and official buck-passing of the present time.

Radlett, Herts. REGINALD S. MURLEY.

SIR,—The logic of Mr. Brearley's letter of Jan. 4 is incontestible. The solution to the senior-registrar problem now and in the future lies in the appointment of more consultants, especially in general medicine and general surgery. However, the Ministry are unlikely to make any movements in this direction without being convinced that the hospital consultant service is in imminent danger of breakdown. Unfortunately, the undoubted shortage of consultants has been obscured since the inception of the service by the fact that most consultants have been working overtime. This habit, which would be condemned immediately by any trade union, seems to be inseparable from a vocational profession. Ironically enough, the Minister is already supplying the remedy in the form of economic pressure, resulting from the steady decrease in the real income of hospital employees. No longer will these doctors be able to subsidise the health service on the scale which has applied in the past. They will be too busy attending to the chores, the repairs, and the decorations at home where adequate help can no longer be afforded. Waiting-lists will grow and the problems in question will be solved much more quickly than they would ever be as a result of the negotiations which are proceeding interminably.

Liverpool. NORMAN GIBBON.

1. *Lancet*, 1957, ii, 1336.

SYRINGES: CLEAN OR STERILE?

SIR,—Your annotation of Jan. 4, drawing attention to the Nuffield Provincial Hospital Trust's book on the planning and organisation of central syringe-sterilisation services, is most welcome, and I hope will further accelerate the spread of such services throughout our hospitals. In terms of economy and preventive medicine, central syringe sterilisation should appeal to lay and medical members of boards of management alike.

It seems timely, too, to consider sterilisation of syringes in public health clinics and general practice, especially on account of the impending inoculation of adults against poliomyelitis.

Mass inoculation campaigns in children, using one syringe, and a different, recently sterilised, needle for each child, have been happily free from the spread of syringe-transmitted hepatitis. In adults, however, such sub-standard technique—excused by some on grounds of practicability—seems likely, in the light of experience, to prove dangerous. There is ample proof in the literature that irrespective, of the type of injection, epidemics of hepatitis are likely to occur in clinic populations where each patient is not served with a sterile syringe and needle. Hepatitis is not generally listed by public health authorities as a notifiable disease, and since its incubation period is long, much harm may be done before the dangers are fully appreciated.

Public health authorities and general practitioners, no less, therefore, than hospitals, would do well to reconsider their sterilisation arrangements, not only in terms of preventive medicine, but also perhaps, since the consequences of using contaminated equipment are well established, from the medicolegal aspect also.

Stockport. R. S. MORTON.

SIR,—Your annotation of Jan. 4 makes no mention of the problems of syringe sterilisation in general practice.

I have obtained a supply of 2 ml. Luer lock syringes with number-17 hypodermic needles mounted and protected by a metal needle guard. These are packed in a cylindrical screw-capped metal container, with a small cotton-wool plug.

The containers are autoclaved for me at my local hospital and I imagine that most hospitals would cooperate with family doctors in this way.

A safe sterile syringe in one's coat pocket, car, or visiting bag, ready for immediate use, with a sterile plug of cotton-wool for skin preparation, is particularly useful when answering an emergency call.

London, S.E.26. R. N. JACKSON.

TUBERCULOSIS IN THE SCHOOL

SIR,—Many will agree with the opening and closing sentiments of your annotation.[1] Certainly the tuberculin test is a very useful tool in investigating the epidemiology of tuberculosis among schoolchildren. Not only does a positive reaction indicate which children need to be examined more carefully and followed, but the identification of those who have been in contact with an infectious case of tuberculosis makes it possible to identify the source case among their current associates. Moss and Fairweather[2] have again demonstrated the great value of this approach to the prevention of tuberculosis.

At the same time, the Clitheroe experience clearly points up a serious disadvantage of B.C.G. vaccination. Aside from the question of the logic of vaccinating the children who were still uninfected after the source cases had been removed, the positive tuberculin reactions engendered by B.C.G. will make a similar surveillance impossible in the future. Is not B.C.G. vaccination under these circumstances rather like killing the goose that laid the golden eggs?

Tuberculosis Program,
Division of Special Health Services,
Public Health Service,
Washington 25, D.C. GEORGE W. COMSTOCK.

HÆMORRHAGE IN LIVER DISEASE: TREATMENT WITH SEROTONIN

SIR,—We have had the opportunity of testing serotonin in three cases of hæmorrhage appearing in the course of severe liver disease.

One patient had juvenile cirrhosis (postmalarial?) with hypersplenism (leucopenia, thrombocytopenia), hæmorrhages and purpura, treated by splenectomy; two had severe and protracted epidemic hepatitis (post-transfusional in one) with a severe hæmorrhagic state characterised by spontaneous ecchymosis.

To estimate the efficiency of serotonin the following tests were carried out before and after the beginning of the treatment with serotonin:

The bleeding-time; the coagulation-time of the venous blood at 37°C (Lee-White); the Rumpel-Leede test after venous stasis at over-diastolic arterial pressure for 5 min.; the clot retraction (serum expressed per 5 ml. blood after 60 minutes in the incubator); and the platelet-count.

Serotonin, 1–2 vials of 5 mg. intramuscularly, was given daily for a few days. It was well tolerated, and produced no local or general reactions, such as were seen after intravenous administration (e.g., tachycardia, hypertension, and dyspnœa). Improvement in the hæmorrhagic state was indicated by cessation of bleeding in the skin and alimentary-tract hæmorrhages. The bleeding-time diminished in all three cases (see table). The coagulation-time improved, the Rumpel-Leede sign became negative, and the clot retraction improved, but the number of platelets remained at the same low level.

From our data it seems that serotonin acts especially on the capillary resistance and clot-retraction without influencing, in the doses used, the number of platelets.

The serotonin was kindly supplied by Messrs. Hoffmann-La Roche.

Hospital of Infectious Diseases,
Colentina, Bucharest, Rumania. NEUMAN MAUR
P. TEODORESCU.

EFFECT OF SEROTONIN ON HÆMORRHAGIC STATE

Patient	—	Bleeding-time	Coagulation-time	Prothrombin time (Quick) (sec.)	Clot retraction (ml. serum)	Platelets (per c.mm.)	Rumpel-Leede test
1	before	4 min. 15 sec.	9 min.	16 (control 12)	1·1	76,000	++
	after	2 min. 30 sec. 2 min. 50 sec.	5 min. 30 sec. 5 min. 10 sec.	15	1·8	72,000 68,000 66,000	±
2	before	3 min. 10 sec.	8 min. 10 sec.	18 (control 13)	1·2	54,000	++
	after	2 min. 30 sec. 2 min. 40 sec.	4 min. 50 sec. 5 min. 10 sec.	17 16	1·9	46,000 38,000 52,000	+
3	before	3 min. 40 sec.	9 min. 50 sec. 5 min. 50 sec.	24 (control 14)	1·0	38,000	+++
	after	3 min. 10 sec. 2 min. 20 sec.	5 min. 40 sec.	23 22	2·4	46,000 42,000 48,000	±

1. *Lancet*, 1957, ii, 784.
2. Moss, P. S., Fairweather, J. H. *Brit. J. Tuberc.* 1957, **51**, 258.

THE DIFFICULT KNEE

SIR,—May I congratulate you on your annotation of Dec. 14? I should, however, like to discuss several points.

(1) A knowledge of the mechanism of injury is essential.

(*a*) A direct injury can cause contusion and bruising of the soft-tissue structures such as the infrapatellar pad of fat, alar folds, synovial membranes, and menisci as well as the articular cartilages and bones of the tibia, femur, and patella. Unless these cases are treated by immediate active methods, including rest from all forms of strain, and appropriate graduated exercises, complications tend to develop which include an unstable knee, a stiff knee, articular cartilage erosion, chondromalacia patellæ, and early joint degeneration. It would seem that too many cases with a history of direct injury are subjected to menisectomy far too soon. The effects of contusion and bruising, if allowed to become chronic, may take many months of treatment to overcome especially if the case has been neglected at the beginning.

(*b*) The components of an indirect injury must be clarified. Was it a purely abduction strain or was there an element of rotation and flexion as well? A hyperextension injury may contuse the infrapatellar pad of fat and involve the structures in relation to the tibial spine as well as stretching or tearing the posterior capsular structures. It should be realised that in an indirect injury the structures on one side of the joint are stretched or torn, whereas those on the opposite side may suffer direct injury and be contused and bruised.

(2) Before operation the stability of the joint must be assessed. One of the menisci may be torn, but the prognosis is entirely different when there is a stable knee and when there is cruciate or lateral ligament laxity. The knee may give way on occasions without true locking and McMurray's tests may be negative, but often, although flexion may appear to be full, a rubbery elastic feeling can be elicited and there is a distinct difference in the feel of the two sides. The patient

appreciates this difference as he can do a full-knees bend on the good side but not on the affected one.

(3) At operation the femoral and tibial articular cartilages must be observed and the patellar one as well if necessary. These findings are important in regulating the tempo of convalescence and rehabilitation. The stability of the ligaments is again assessed under anaesthesia and direct vision. A recent case illustrates this point:

A young rugger player aged 17 showed signs of a torn medial meniscus of the right knee. At operation there was no evidence of articular-cartilage damage and the ligaments were normal. He made a quick convalescence and had no trouble with this knee. Three years later he injured his left knee while parachuting and the knee continued to give way on several occasions. At operation, apart from the tear of the medial meniscus there was evidence of early erosion of the articular cartilage on the medial condyle. This knee now is returning to full function slowly.

In a case of this sort it is essential not to force strenuous activity.

(4) Chondromalacia patellæ is certainly a common sequel to any injury of the knee-joint, but it often occurs in childhood and adolescence from no apparent cause. These cases can often be kept in circulation by modifying one of their activities such as avoiding P.T. and Corps work at school but allowing cricket and even football. They should wear sponge-rubber heels to avoid jarring and carry out conscientious daily home treatment and physiotherapy, first as a course and later once a week. Without treatment the condition progresses and may require operation. Occasionally, in spite of great care operation may be inevitable.

(5) Every case of injury to the knee-joint, especially a joint in which menisectomy has been performed, is a potential case of osteoarthritis. The early physical signs of this condition are articular cartilage rolling and synovial thickening. Sometimes in these latter cases even radiographs show a normal joint, but this constitutes the pre-X-ray phase of osteoarthritis and is reversible with appropriate treatment. Removal of a meniscus may be necessary in a middle-aged man associated with early osteoarthritis but it must be remembered that the operation itself gives three weeks' rest from strain and in the more advanced osteoarthritis simple removal of the meniscus does not make them symptom-free. The patient is warned of the likelihood of osteoarthritis and if he will only persist with regular home treatment indefinitely he can delay the onset. This claim will be open to criticism but many patients in whom osteoarthriits has developed have been helped by home treatment and courses of physiotherapy and lose their physical signs and symptoms. If a claim for a cure for osteoarthritis had been made 20 years ago the doctor would be considered a charlatan, but since it has been proved that articular cartilage can regenerate patients showing early osteoarthritis can themselves become symptom-free. It is essential in these cases, however, for the patient to continue home treatment indefinitely.

(7) In about 2–5% of cases in which the diagnosis is difficult and in doubt, I have always found that arthrograms, as carried out by Somerville, have supplied the answer in almost every case. As performed by him this is a method without danger.

(8) Few textbooks draw attention to the secondary effects on the joint above and below the injury. Such muscles as the hamstring and adductor magnus affect the movements of the hip as well as the knee, and in knee injuries they tend to contract and shorten. This also applies to the calf muscles and their effect on the movements of the ankle-joint. Full extensibility and flexibility of the muscles must be restored with full movements of both ankle and hip as well as the knee before the patient can expect to have a knee which is 100%. No patient with a knee injury should be labelled "functional" until full movement has been obtained in the hip, knee, and ankle joints as well as restoration of full muscle power. To obtain this the knee may have to be subjected to a series of controlled manipulations under thiopentone, as well as long courses of physiotherapy including gentle manipulations.

London, W.1 W. E. TUCKER.

ENZYME TESTS FOR GLUCOSE

SIR,—May I support Dr. Miller's view (Jan. 11) of the reliability of the enzyme tests ('Clinistix' and 'Testape') as a means of detecting, but not measuring, urine-glucose?

The 11% of discrepancies found by Tunbridge et al.,[1] and quoted in *Prescribers' Notes* (May, 1957), arises from the assumption that a negative reaction with 'Clinitest', or other copper-reduction tests, means that glucose is absent, whereas the true position is that the enzyme tests can detect a lower level of glycosuria than can clinitest, though the clinical significance of such a trace of glucose may be slight.

Reducing sugars other than glucose are not, of course, detected by the enzyme tests, but I have encountered only two substances which give false-positive reactions—namely, hydrogen peroxide and hypochlorites. The first is largely of theoretical interest, but many household and laboratory cleansers contain hypochlorites, and false positive reactions can arise from gross contamination of urine containers.

I should be very interested to hear of a positive reaction in uncontaminated urine, where glucose was proved to be absent—e.g., by paper chromatography.

The specificity of glucose oxidase is not in dispute, and false-positive reactions are more likely to arise from substances capable of oxidising *o*-tolidine to give the blue pigment. So far as I am aware, no such substance has been found in urine.

Department of Clinical Chemistry, Royal Infirmary, Edinburgh SAMUEL C. FRAZER.

POSTOPERATIVE VENOUS THROMBOSIS

SIR,—Your leader of Nov. 30 and Dr. Rivlin's letter (Dec. 21) draw attention to the need for active movement in the lower limbs in the prevention of venous thrombosis in recumbent patients, and as a necessary supplement to anticoagulants in the treatment of established venous thrombosis.

Many patients, however, are in need of exercise, but unfit to get up. Encouragement to move about in the bed, or to keep the lower limbs moving, is often insufficient to ensure adequate venous return, and many are naturally apprehensive lest they injure themselves or their operation wounds. There are special

1. Tunbridge, R. E., Paley, R. G., Coulson, D. *Brit. med. J.* 1956, ii, 588.

indications for actively exercising the legs in thrombophlebitis, and where venous thrombosis is feared after operation or during long recumbency. For this reason a leg exerciser was devised, the objects of which were:

To allow movement against resistance, both at the ankles and knees, which the patient could continue to perform as required and without undue fatigue.

To provide suitably padded pedals without danger of damage from friction or pressure over the skin of the heels or elsewhere.

To make the apparatus portable and easily accommodated in a hospital bed beneath the bedclothes.

The accompanying illustration shows the apparatus made for this purpose by the engineers' department at the Queen Elizabeth Hospital, Birmingham. It was adapted from a standard bed-cradle, into which were built brackets to hold pedals suspended from above, hinged at suitable points, and attached to the cradle by springs, thus providing resistance to both ankle and knee movements. Hooks were so fitted that the sites of attachment of the springs to the cradle itself could be changed, and their tension readily adjusted to suit the requirements of each patient.

This apparatus has proved acceptable to patients, comfortable in use, and of value in retaining muscle tone in recumbent patients. It should be helpful in preventing postoperative and other thrombophlebitic complications, and, in conjunction with anticoagulants, accelerating the resolution of œdema of the legs in established cases of venous thrombosis.

I am indebted to Mr. T. F. Dee, clinical photographer at the Queen Elizabeth Hospital, Birmingham, for the illustration, and to the engineering departments of the Queen Elizabeth and General Hospitals, Birmingham, for making the apparatus.

Edgbaston, Birmingham. G. E. OWEN WILLIAMS.

SANATORIA BEDS

SIR,—In matters of medical treatment the pendulum of fashion is apt to swing too far and too fast. Dr. Beresford's letter (Jan. 4) is an example of this. He can see no good in the larger sanatoria, where education of the patient, said by him to have little scientific basis, is still thought to be an essential part of treatment and rehabilitation. Furthermore, such treatment is said to breed hypochondriacs. Nothing could be further from the truth. Considerable experience on both sides of the blanket has convinced me that the valetudinarian is a product of long domiciliary treatment. The patient idling around at home loses a sense of purpose much more rapidly than the sanatorium inmate whose graduated activity is leading steadily on towards return to normal life and employment.

Reading Dr. Beresford's letter, one would think that the large sanatorium had nothing to offer except rules and regulations. What about laboratory facilities, resident staff, and surgical units? It seems to me that many people have reached the erroneous conclusion that the treatment of pulmonary tuberculosis has become just too easy since the discovery of streptomycin—a conclusion which may be responsible for the increasing number of patients admitted to sanatoria harbouring resistant strains of the tubercle bacillus. I have the good fortune to work in an area where adequate admission to hospital is still the treatment of choice in newly discovered cases, and as a result the proportion of resistant strains is below average. It is still high enough to make the use of all three standard drugs advisable at least until the sensitivity of the strains are known. 60% of our tuberculous admissions are still open cases.

Presumably I am one of the "interested parties" who are striving to maintain the larger sanatoria. But what of Dr. Beresford? Are there also interested parties striving to maintain the smaller units?

Cheshire Joint Sanatorium, Market Drayton, Salop. A. CLARK PENMAN.

Obituary

WALTER ELLIOT

P.C., C.H., M.C., M.B., D.Sc. Glasg., LL.D., F.R.C.P., F.R.S., M.P.

THOUGH Walter Elliot was one of our rare medical Ministers of Health, in this and in the other high offices which he held he acted as a statesman with a medical background rather than as a doctor with an interest in politics. Nevertheless his work at Westminster and Whitehall was firmly based on medical knowledge and biological principles, and if the marriage which he proposed between health and agriculture was politically convenient it was also a real contribution to the nutrition of a nation that was at that time, at least partially, malnourished.

He was born in 1888, the son of William Elliot, of Muirglen, Lanark. From Glasgow Academy he entered the University of Glasgow. There, with O. H. Mavor, later better known as James Bridie, he had his first taste of politics in the light-hearted rectorial elections. (He once wrote a song in Welsh in support of Lloyd George, who was an unsuccessful candidate.) With Mavor he turned the undergraduate *Glasgow University Magazine* into a publication which became the envy of almost every other university. His popularity was shown by his unanimous election as president of the union. He shone at dinners or suppers and could lift the dullest of occasions into the realms of hilarity, for he was a brilliant "off the cuff" speaker. Like Mavor, he recognised the value of ridicule as a weapon. "Each of them," a contemporary recalls, "delivered his thrusts with a smile, but Elliot's arrows were more difficult to pull out. If, in argument, he was a formidable opponent, he could give and take with equal grace and charm." After graduating B.SC. in 1910 and M.B. in 1913 he was a resident in the Glasgow Royal Infirmary before he joined the R.A.M.C. From 1914 to 1918 he served in France, winning the Military Cross and bar.

Universal Pictorial Press

Almost immediately after demobilisation Elliot was elected Unionist M.P. for Lanark, and his links with medicine began to slacken. For a time he served on the public-health staff of a London borough. A period of research on animal nutrition at the Rowett Institute (when John Boyd Orr was the chief) earned him the D.SC. in 1923. But thenceforward the main thread of his life lay in politics. He held junior offices in the Scottish Department, the Ministry of Health, and the Treasury during the '20s. In 1932 he became Minister of Agriculture, in 1936 Secretary of State for Scotland, and in 1938 Minister of Health. The quality of his work on the front bench and on the back benches of the House of Commons are shown by these tributes from a Civil Servant and from a fellow M.P.:

Elliot's stay as Minister of Health was all too brief, for he left in 1940 when the plans for the Emergency Medical Services and evacuation were beginning to prove their value, and when his experience and driving force would have further enhanced his reputation as an administrator. But Ministers

of Health come and go, and Elliot bore his disappointment with equanimity.

On visits of inspection in England and Wales he was a delightful companion, keenly interested in everything and enjoying temporary release from his desk. He worked hard, too hard we thought sometimes, for he never spared himself. He took a special interest in nutrition, fostered by his experience as Minister of Agriculture, and I recall many talks with him and Lord Boyd Orr. New knowledge of the subject, partly through Elliot's influence, was embodied in the Government's rationing scheme.

It is difficult to realise that he has gone from us. That tall figure so full of vitality, enthusiasm, and brilliance, that fluent speech adorned with Scottish accent, wit, and humour, that desire to serve his country which led him to arduous missions abroad, and also to represent his Sovereign as Lord High Commissioner to the General Assembly of the Church of Scotland—all these seemed so essential a part of the national life.

A. S. M.

To most of us who were his contemporaries in Parliament, Walter Elliot will be remembered rather as an influential back-bencher than as a Minister and scarcely at all as a doctor. "Colonel Elliot" frequently, "Mr. Elliot" often, "Dr. Elliot" hardly ever. That he had an abiding interest in and affection for his first profession, medicine, there can be no question. He served effectively as Under-Secretary for Health at the Scottish Office and as Minister of Health in Whitehall. Yet he gave the impression that he was mindful of the saying current before his time in the Ministry that "doctors do not make good Ministers of Health" and preferred to base himself on a Parliamentary rather than a medical reputation. He was not outstandingly active in the negotiations and debates over the National Health Service Bill. But his position in recent years as a vigorous and respected back-bencher is unassailable and he was prominent in the discussions in the Conservative "1922 Committee". The niche he cut for himself was as an interpreter of back-bench opinion to Cabinet Ministers and as an interpreter of the Cabinet to the parliamentary party. He could speak with freedom in both circles, knowing that his opinions would be listened to. I can recall more than one occasion when tensions were resolved by his intervention at party meetings.

His capacity for friendship, his wise and well-stored mind, and his exceptional experience meant that he was often called to head delegations and to speak as a representative parliamentarian. This was a role in which he seemed more at home than in the rough and tumble of party politics—though he never disdained the dust and turmoil of party conflict—and will be the contribution to the work of the House of Commons for which he will be gratefully remembered by those who worked with him. The House needs a handful of statesmen free to move at need above the arena of our daily concerns. Walter Elliot, by his natural endowments, his personality, and his experience was one of these. The House has too few of them and his death is a real loss.

H. L.

Though Elliot did not return to Ministerial office after 1940, as these tributes show he continued to give much valuable service. One of his interests in these last years linked him once more directly to medicine, and of his presidency of the Royal Institute of Public Health and Hygiene J. B. A., who had known him since they were both students in Glasgow, writes:

Immediately after the first world war I, then an R.M.O. at the Royal Chest Hospital of London, renewed my acquaintance with Walter Elliot who, though his foot was on the first rung of the political ladder, was at that time interesting himself in public health and acting as a part-time assistant to a medical officer of health in a London borough. We had many conversations over lunch at the hospital and I was impressed with the keen interest which he took in preventive medicine. Later it was my privilege as a member of council of the institute to approach Elliot to ascertain whether he would be willing to become our president. It was characteristic of the man that he did not accept this office before acquainting himself with the work and activities of the institute. From his election in 1946 he was not only a figurehead but an active president, and on many occasions he addressed from the chair the fellows and members.

Behind the public figure there remained the man, and of him his friend T. J. H. writes:

Walter Elliot carried his sense of fun through every phase of his career. His interests were multiple and if he took up a subject he made it his business to master it. He was a friendly man, and although as a public figure he had his critics, over the years he never lost his capacity for making and holding friendships. The distinctions and honours which were conferred on him reflect in some measure the great services so cheerfully given in and out of office, academic and political. He was bound to meet with disappointments and frustrations, but he appeared to regard them as part of the art of living, and never permitted sourness, bitterness or regret to mar his countenance or speech. A very full life has reached its close. In many and different circles, particularly in Scotland where he was respected, admired, and loved, it will be a long time before we become accustomed to the idea that Walter Elliot is no longer with us.

Elliot died on Jan. 8 at his home in the Borders and is survived by his second wife, formerly Miss Katharine Tennant.

Miss EDITH HALL

H. M. M. M. writes:

Edith Hall was elected obstetric surgeon to the Mothers' Hospital, London, in 1923. She held this post for about 26 years and was latterly chairman of the medical committee. Her warm human kindness, understanding, and integrity earned the affection of all who knew her, and her obstetric and gynæcological skill and judgment won the confidence of those who worked for or with her. At the end of a hectic day, one of her registrars remarked that when obstetric emergencies and anxieties piled up in the wards and labour-rooms, the arrival of Miss Hall in the hospital brought immediate relief and a sense of calm—a spontaneous tribute which reflects the remarkable influence she possessed, as well as being a tribute to her outstanding ability as an obstetrician. Her wisdom and personality were a valued asset both to the Mothers' Hospital and to her colleagues, and her resignation, when she found her professional burden too heavy, was a lasting loss. The sympathy of all who knew her goes out to her sister and close friend, Dr. Marjorie Hall.

Appointments

BEIRNE, EILEEN M., M.B. N.U.I., D.C.H., D.P.H.: assistant divisional M.O., Lancashire.

JACOBS, RACHEL, M.D. Prague, D.P.H., D.OBST.: assistant M.O. (administrative), West Ham.

MCNAMARA, HILDA E., L.M.S. Newfld., D.P.H., D.OBST.: assistant divisional M.O., Lancashire.

MANN, G. E., B.M. Oxon., F.R.C.S., D.L.O.: part-time consultant E.N.T. surgeon, Chesterfield Royal Hospital.

MARTIN, ALBERT, M.B. Birm.: assistant M.O.H., Sutton Coldfield.

PINKERTON, ISABELLA M., M.B. Wales, D.P.H.: assistant M.O., High Wycombe area.

TWEEDY, P. S., M.D. Lond., M.R.C.P.: physician (S.H.M.O.), geriatric unit, Newcastle group of hospitals.

Births, Marriages, and Deaths

DEATHS

MEREWETHER.—On Jan. 7, at the Royal Victoria Hospital, Folkestone, Henry Osborne MacCabe Merewether, O.B.E., F.R.C.S.E., of Lympne Hall, Lympne, Kent.

Notes and News

CONTROL OF NARCOTICS

IN its report [1] for 1957, the Permanent Central Opium Board of the United Nations says that the operation of the system of control of narcotics has improved in the past five years; statistics have been fuller, more accurate, and more promptly submitted, though some countries cooperate less well than others. The board deals with *all* narcotic drugs.

One of the effects of the controls introduced in 1925 and 1931 has been that it is now almost impossible for addicts to get narcotics from legal sources. The legal production is virtually limited to medical and scientific needs, except in the case of coca leaves and cannabis; the quantity of coca leaves produced for chewing is unknown but was not less than 9600 tons in 1956 (thirty times the production for medical use). From 1955 to 1956 the quantity of opium produced decreased, while the amount used in medicine increased. Only three countries manufactured heroin in 1956, and the international trade was negligible (1 kg.). 32 synthetic narcotic drugs were controlled by 1956; pethidine is by far the most commonly used, the United States accounting for two-thirds of world consumption.

NOTIFICATION OF ACUTE RHEUMATISM

UNDER the Acute Rheumatism Regulations, 1953, the disease must be notified in Cornwall, parts of Lindsey, the county boroughs of Bristol, Grimsby, Hull, Lincoln, Salford, and Sheffield, and the borough of Ilford. These regulations have now been extended indefinitely. It is possible, the Ministry of Health says, that the areas in which the disease is notifiable may later be increased.

LESSONS IN REPRODUCTION

THERE has appeared a sprightly little picture-book [2] of first lessons in human reproduction and sex for four-to-eight-year-olds and their parents. The line drawings, by Gerda Nystad, of children and young adults, clothed and naked, are modest and pleasing, and the text shows well how to say enough and not too much to the inquiring child. The sketch of the unborn at ease in a womb without exit but pierced by an umbilical feed-pipe seems a little fanciful in such factual context, but the book should both please and profit those it is meant for.

NEW MEDICAL FILMS

Acidity, Dyspepsia, and Peptic Ulcer (16 mm., sound, colour, 28 min., Britain, 1957) presents dyspepsia as an imbalance between gastric acidity and tissue resistance.

It shows that statistically there is a relationship between acidity and the incidence of peptic ulcer, but ulcers that arise where acidity is normal indicate a low tissue resistance. Methods of measuring gastric acidity are shown and the histamine response is described. In the second half of the film the cause of pain is considered and methods of reducing the acidity mentioned. Finally, the advantages are set out of a proprietary preparation for this purpose.

The film gives a concise exposition on the modern view of dyspepsia but the emphasis on a particular treatment detracts from the value of the film for teaching purposes. The commentary is excellent and carries the weight of the exposition. The picture is largely diagrammatic and at times the artist seems to be hard pressed to fill the screen with appropriate symbols to match the lecture. The film may be obtained free from C. L. Bencard, Ltd., Minerva-road, Park Royal, London, N.W.10.

The Manchester Regional Hospital Board is responsible for a film, *There was a Door* (35 mm., sound, black and white, 30 min., Britain, 1957), on mental deficiency.

Taking as its text " It is not in the best interests of patients fit to live in the general community that they should live in large and remote institutions—cut off from the world " (from the report of the Royal Commission on Mental Illness) the film discusses the problem of the overcrowding of hospitals with mentally deficient patients, many of whom could be trained to undertake suitable work and live at home. The training centre at Oldham is described, and municipal and county authorities are encouraged to set up similar centres for the training of mental defectives in their areas.

The film puts extremely well the case for keeping mentally defective patients out of hospital; this coincides with the recommendation of the Royal Commission, though the film was in production before the report was published. The film is designed primarily for local health authorities, and it is therefore surprising that some patients with extreme mental deficiency, who are unsuitable for training, are shown in the film. Indeed the film should be very carefully introduced when shown to non-medical audiences. The production is of professional standard. The film is available on hire from Sound Services, Ltd., 269, Kingston Road, London, S.W.19. 16 mm. prints will probably be available shortly.

Nobecutane—A Plastic Surgical Dressing (16 mm., sound, colour, 23 min., Britain, 1957) describes the properties and uses of the plastic skin dressing in surgery and other fields.

The film mentions its advantages over conventional dressings, and shows in detail its application to an operation wound and the subsequent removal of sutures. Other varied situations are named where the dressing has proved valuable, and the film ends with a summary of its properties.

This is a very good film that convincingly presents the advantages of the plastic dressing. A black and white sequence of the Korean war could be omitted, but otherwise the pictures and commentary contribute equally to the smooth exposition. The colour photography is excellent and the commentary authoritative and clear. The film is available free from the Film Library, Evans Medical Supplies, Ltd., Liverpool.

1. Permanent Central Opium Board: Report to the Economic and Social Council on the Work of the Board in 1957. United Nations, Geneva, 1958. Pp. 83. 5*s*. 6*d*. Obtainable from H.M. Stationery Office, P.O. Box 569, London, S.E.1.
2. Peter and Caroline. A child asks about childbirth and sex. By STEN HEGELER. London: Tavistock Publications Ltd. 1957. Pp. 29. 7*s*. 6*d*.

University of London

On Dec. 18 the degree of M.D. was conferred on F. W. O'Grady.

University of Bristol

The following have been approved for the degree of M.D.:

A. J. Coppen, D. G. Davies, G. Walters.

Order of St. John of Jerusalem

The Queen has sanctioned the following promotions in, and appointments to, this Order.

As Knights.—J. T. Whitley, O.B.E., M.B., R. V. S. Cooper, M.B.

As Commanders (Brothers).—Sir Geoffrey Todd, K.C.V.O., O.B.E., F.R.C.P., Sir Charles Dodds, M.V.O., F.R.C.P., F.R.S., D. P. McIntyre, F.R.C.S.E., J. C. R. Buchanan, C.M.G., M.D., F.R.C.P., C. H. Drake, M.R.C.S., D. W. Montgomery, M.D., F.R.C.S.I., M. Y. Paget, M.R.C.S., Air Vice-Marshal L. M. Corbet, C.B.E., M.B., George Swapp, D.C.M., M.M., M.B., H. H. Hurst, M.B.

As Officers.—H. D. Teare, M.B., Squadron-Leader Philip Cauthery, M.B., William Duncan, M.B., C. T. Newnham, M.R.C.S., Alexander Morrison, L.R.C.P., Alexander Chalmers, M.B., C. F. Fairlie, M.D., T.D., A. G. Walker, M.B., R. G. Sprenger, M.B., R. H. Kipping, M.B., R. H. Scott, M.R.C.S., S. W. Cooper, F.R.C.S., J. H. C. Clarke, M.B., G. N. M. Wishart, M.R.C.S., F. P. Wallis, M.R.C.S., S. G. Nelson, M.B., J. M. Pedler, M.B., N. G. Hoddle, M.B., M. F. Leslie, M.B.

Royal Commission on Remuneration

The Royal Commission on Doctors' and Dentists' Remuneration will hold a public hearing on Thursday, Jan. 23, at Church House, Great Smith Street, London, S.W.1, at 11.15 A.M. Representatives of the British Medical Association have been invited to attend.

International College of Surgeons

Forthcoming meetings of the college include a scientific trip to the United States, leaving about March 1 and returning about March 22, and a meeting in Brussels from May 15 to 18. Further particulars may be had from Dr. J. F. Brailsford, 20, Highfield Road, Edgbaston, Birmingham 15.

World Federation for Mental Health

On Jan. 24 Dr. Brock Chisholm, president of the World Federation for Mental Health, will speak at Leeds on Human Problems of the Atomic Age. This will be the annual public lecture arranged by the United Kingdom committee of the Federation. It will be given in the great hall of the University of Leeds at 6 P.M., and tickets may be had for 2*s*. 6*d*. from the northern secretary, National Association for Mental Health, 9, Mount Preston, Leeds, 2.

Royal College of Surgeons of England

At a meeting of the council on Jan. 9, with Sir James Paterson Ross, the president, in the chair, Mr. B. K. Rank, of Melbourne, was appointed Sir Arthur Sims Commonwealth travelling professor for 1958. Dr. G. S. W. Organe was appointed Joseph Clover lecturer for 1959.

Dr. C. A. Keele was elected to the fellowship of the Faculty of Anæsthetists. A diploma of fellowship was granted to A. B. Cassie, and a diploma of membership to V. P. Nagpal.

The following diplomas were granted jointly with the Royal College of Physicians:

D.L.O.—Paul Abbey, Rasheed Ahmad, Z. H. Alvi, Julian Bihari, Thomas Cartmill, R. R. A. Coles, B. R. Das, M. J. D'Cruz, J. L. Golden, John Hall-Jones, Martin Horowitz, Y. P. Kapur, G. M. Khan, F. W. Kwok, Ishwar Narain, N. B. Parvathiah, Jeffery Potter, L. N. Prasad, Rajendra Prasad, I. P. C. Robertson, D. S. Sardana.

D.A.—F. D. Adrianvala, Eleanor K. Althorp, Edna W. Anthony, N. K. Ashurst, Roma M. Bedford, Abraham Berry, Jane I. K. Binnie, H. L. Blake, Margaret A. E. Boyce, J. H. Breed, R. A. Butler, P. H. Byles, Joan M. Byrne, Po Sing Chau, J. M. Clark, R. J. Clark, W. H. Cochrane, G. F. Conway, S. K. Coombes, H. B. Coulter, Bridget M. Cowley, H. J. L. Craig, J. P. Czyniewski, M. A. de Valero Wills, B. J. Dolan, R. R. Evans, A. D. J. Farquharson, M. E. Fielding, G. Flowers, H. J. Freedman, B. L. Gupta, V. G. Gurjar, Christopher Gyaw, R. W. Hall, D. D. Hart, D. F. Hogan, Margaret C. Holderness, W. G. Holland, Ann Horsburgh, T. H. Howells, Ayesha S. Ishrat Husain, M. O. N. Iyengar, T. E. Jones, V. R. Jones, Kathleen E. Kennedy, J. C. Kennedy Smith, J. D. Kinnell, R. J. Knight, H. P. Lacey, R. Grove Lacey, Anatol Lagowski, G. L. F. Lau, P. D. Lawler, J. L. Layng, Phyllis L. Liddle, G. J. M. Lincoln, J. V. McCooey, P. W. McCormick, S. W. McGowan, N. N. Madan, R. E. W. Manley, R. R. Manning, Maung U Win, T. W. P. Millar, J. S. Miller, Mary H. Miller, D. R. Morgan, Ada C. Morrison, Joyce Newman, B. A. Nixon, Krishnapathee Parbhoo, T. F. J. Parker, A. S. Paton, P. A. P. Pompa, Diana Ratcliffe, D. D. G. Simpson, Chanan Singh, Harold Slomowitz, J. A. Stainton-Ellis, K. D. Stephenson, C. R. Sulochana, N. S. Thomas, J. S. Toner, Patricia A. Topham, Sohrab Rustomji Umrigar, R. D. Unkles, Sariphorn Vanikieti, F. H. Walter, Elizabeth M. B. Watson, A. I. Weinreich, J. M. S. Whiting, D. C. M. Wilcox, P. F. Willis, J. E. York, Freda Young.

D.M.R.D.—D. A. Alderson, Keith Ashcroft, Kyaw Aung, W. R. Barrow, D. C. Bernstein, M. P. Bhalla, Savas Bissylass, H. J. Bloch, Ronald Cable, D. F. Cantwell, George Cohen, I. D. Davies, M. L. Dyson, R. F. Fouche, John Fraser, R. W. Galloway, J. J. Gately, Kenneth Grainger, Ian Isherwood, Naphtali Joffe, Brigid Keane, J. T. Lamb, James Lees, J. J. D. Lobo, A. B. McGrigor, M. R. H. Mahmood, R. C. Michell, N. L. Mills, Israel Movsas, N. D. C. O'Connell, Irmgard Patton, J. J. Prior, K. D. Reddy, Percy Reichman, Broughton Ridgway, J. H. Rustage, Ahmed Sardar, H. M. Saxton, S. N. Sender, M. P. Shannon, Eli Sheville, M. J. Strachan, H. M. Strathern, D. F. Street, Geoffrey Sullivan, S. N. B. Talwatte, Sneh Taneja, R. P. Vass, Peter Ward, W. L. Wong.

D.P.M.—G. H. Armitage, Grace Bainbridge, A. H. Borowitz, A. M. Bradfield, S. W. G. Caseley, M. R. Chaudhry, A. B. Cooper, F. H. Corbitt, J. McK. Davie, R. N. Davis, Joseph Erulkar, G. W. Fenton, Albert Gage, M. E. Grant, Ian Hadfield, Lewis Harris, Peter Hays, G. A. Heasman, Mary K. P. Henderson, William Leggat, Kypros Loucas, N. C. Low, S. M. Macentee, N. K. Macrae-Gibson, W. K. Marshall, Pamela G. L. W. Mason, W. J. Nicholson, V. R. Ntsekhe, P. M. J. O'Brien, J. R. Palmer, Barbara Petrovskaia, Abe Pick, E. W. Poole, J. H. Price, J. R. Roy, Barbara J. Salisbury, G. H. Scott, J. C. Scott, Karam Singh, W. B. Spry, J. S. Stead, A. A. Sugerman, S. S. Syalee, W. D. Wilson, Waclaw Wollen.

D.T.M. & H.—H. F. McElligott, Umasanker Sahay, Thambo Tharmaratnam.

D.Path.—B. B. Beeson, P. W. J. Bosman, S. M. Deoras, Geoffrey Garrett, Barbara E. Grahame, I. J. Hunter, Felix Kurrein, C. J. McDonald, James Ward.

D.P.H.—Mary M. M. Boyd, M. J. Catton, M. L. Graeme, Bashir Hussain, P. V. Krishnamurti, C. L. Milburn, S. K. Sen, Tin U, E. J. Wright.

National Association for Mental Health

This association is holding a conference on the report of the Royal Commission on the law relating to mental illness and mental deficiency, on March 6 and 7, at Church House, Westminster, S.W.1.

The speakers will include Dr. W. A. L. Bowen, Dr. D. H. Clark, Dr. J. D. Kershaw, and Dr. Denis Leigh. Further particulars may be had from the conference secretary of the association, 39, Queen Anne Street, W.1.

Chronic Rheumatic Diseases

A weekend course with lectures, ward rounds, and practical demonstrations will be held at the rheumatism unit of St. Stephen's Hospital on March 15 and 16.

Professor J. Trueta will open the course, and the speakers will include Dr. Francis Bach, Dr. Grace Batten, Dr. Raymond Daley, Dr. Philip Ellman, Mr. H. E. Harding, Dr. F. Dudley Hart, Dr. R. H. Marten, Mr. G. Pritchard, and Dr. Gordon Signy. Further particulars can be obtained from the secretary, Fellowship of Postgraduate Medicine, 60, Portland-place, W.1.

Appointment in Northern Ireland

Dr. W. McCartan, who recently retired from the post of physician-superintendent of St. Francis and Hurstwood Park Hospitals, Haywards Heath, has been appointed medical inspector of mental hospitals in Northern Ireland in succession to Dr. F. G. L. Barnes.

International Congress of Physiological Sciences

This congress will be held in Buenos Aires from Aug. 9 to 15, 1959. Further particulars may be had from the secretary, Facultad de Ciencias Medicas, Paraguay, 2151.

London Skin Hospital

In accordance with the decision of the North West Metropolitan Regional Hospital Board, this hospital will be closed for the treatment of skin conditions on March 31. Patients still under treatment at that date will be referred to their general practitioners. New patients will not be accepted after Feb. 14.

Dr. J. A. Fraser Roberts has been elected president of the Royal Anthropological Institute.

CORRIGENDUM: *New Year Honours.*—We regret that through our mistake the name of Dr. Clarence Smith appeared twice in our list of medical honours (Jan. 11, p. 100). Dr. Smith in fact was appointed O.B.E.

Diary of the Week

JANUARY 19 TO 25

Monday, 20th

HUNTERIAN SOCIETY
8.30 P.M. (Mansion House, E.C.4.) Sir Ernest Rock Carling: Biological Systems and Atomic Radiation. (Hunterian lecture.)

Tuesday, 21st

ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
8 P.M. *Pathology.* Prof. J. Firket (Liège): Cancer of the Lung in the Industrial Area of Liège during Recent Years.

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine, Keppel Street, W.C.1.) Dr. L. H. Gray: Influence of Oxygen on the Response of Cells and Tissues to Ionising Radiation.

ST. MARY'S HOSPITAL MEDICAL SCHOOL, W.2
5 P.M. Prof. Charles Rob: Ileus.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
5.30 P.M. Prof. F. C. Ormerod: Sinusitis.

INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. R. H. Mears: Skin Diseases in Children I.

SOCIETY FOR THE STUDY OF ADDICTION
8 P.M. (11, Chandos Street, W.1.) Sir Adolphe Abrahams: Use and Abuse of Drugs by Athletes.

MANCHESTER MEDICAL SOCIETY
4.30 P.M. (Medical School, University of Manchester.) Prof. Robert Platt, F.R.C.P.: Darwin, Mendel, and Galton.

UNIVERSITY OF ST. ANDREWS, Queen's College, Dundee
5 P.M. Prof. A. E. Ritchie: Methods of Artificial Stimulation and Potential Recording in Neuromuscular Disorders.

Wednesday, 22nd

ROYAL SOCIETY OF MEDICINE
5 P.M. *Endocrinology.* Dr. Sheila Sherlock, Dr. Julius Lee, Dr. G. W. Bisset, Dr. W. H. Summerskill: Endocrine Changes in Liver Disease.

POSTGRADUATE MEDICAL SCHOOL, Ducane Road, W.12
2 P.M. Dr. R. R. Race: Contributions of Blood Groups to Human Genetics.

INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Sir Russell Brock: Basic Principles in Heart Surgery.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. Henry Haber: Cellular Nævi.

NOTTINGHAM MEDICO-CHIRURGICAL SOCIETY, 64, St. James's Street, Nottingham
8.30 P.M. Dr. C. A. Boucher: Accidents in the Home.

MANCHESTER MEDICAL SOCIETY
4.30 P.M. (Medical School.) *Medicine and Pathology.* Prof. Alexander Haddow: Recent Trends in Cancer Research.

Thursday, 23rd

UNIVERSITY COLLEGE LONDON, Gower Street, W.C.1
5 P.M. Dr. E. Lester Smith: Biochemical Functions of Vitamin B_{12}.

ROYAL SOCIETY OF MEDICINE
8 P.M. *Urology.* Prof. N. F. Maclagan: Urinary Colloids. Mr. J. H. Carver: Bilateral Orchidopexy and Fertility. Mr. Norman Slade: Bacteræmia and Septicæmia after Urological Operations.

BRITISH POSTGRADUATE MEDICAL FEDERATION
5.30 P.M. (London School of Hygiene and Tropical Medicine.) Mr. A. F. Huxley: Excitation and Contraction in Voluntary Muscle.

INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. Mears: Skin Diseases in Children II.

NUFFIELD ORTHOPAEDIC CENTRE, Wingfield-Morris Orthopædic Hospital, Oxford.
8.30 P.M. Dr. J. D. Mineiro: Arteriography in Orthopædic Surgery.

LIVERPOOL MEDICAL INSTITUTION, 114, Mount Pleasant, Liverpool, 3
8 P.M. Dr. Philip Robinson, Dr. A. Thelwall Jones, Dr. Leonard Findlay: Care of the Aged.

UNIVERSITY OF ST. ANDREWS, Queen's College, Dundee
5 P.M. Prof. H. P. Gilding: Capillary Circulation and Tissue Fluid Exchange.

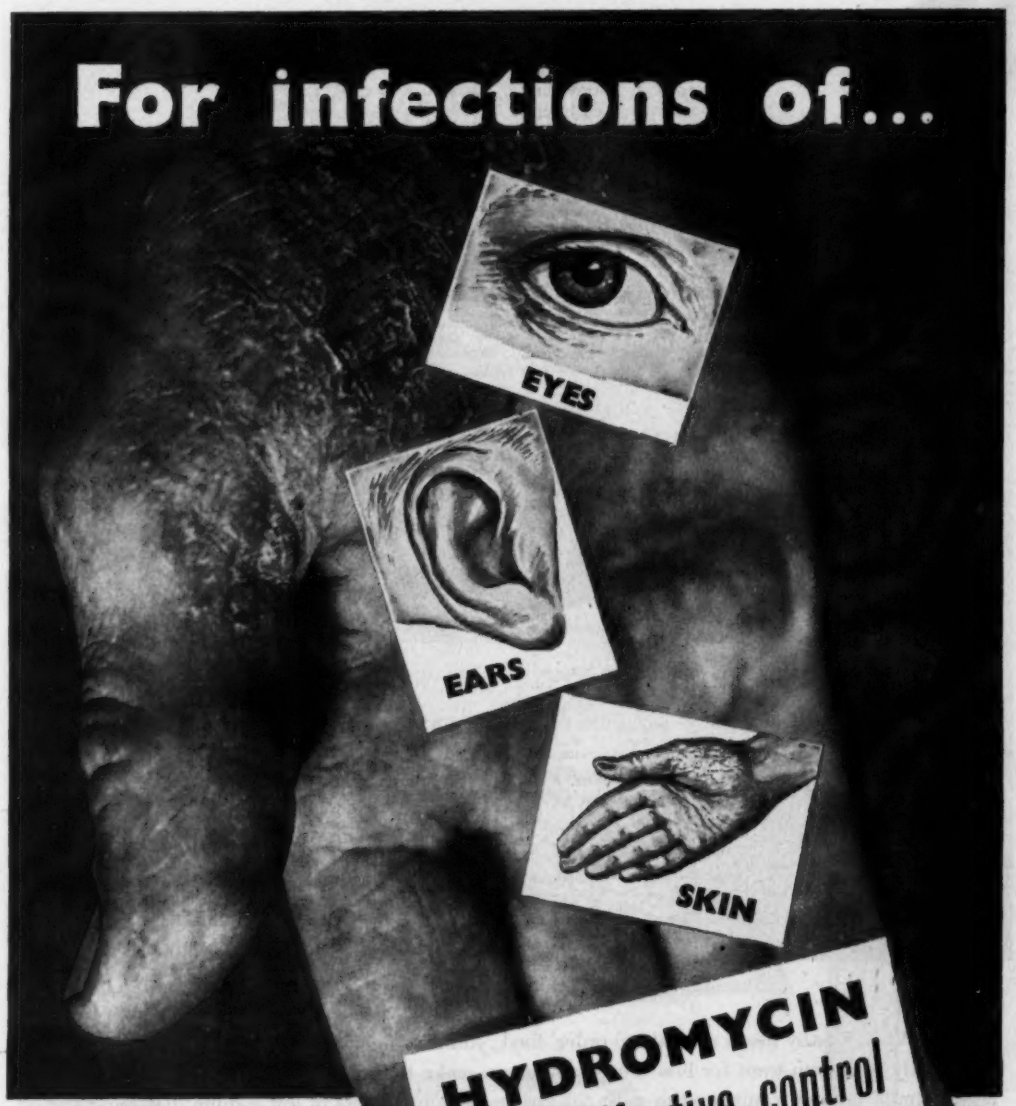
Friday, 24th

ROYAL SOCIETY OF MEDICINE
5 P.M. *Pædiatrics.* Dr. C. A. Boucher, Mr. Douglas Jackson: Prevention of Accidents in Childhood.

POSTGRADUATE MEDICAL SCHOOL
10 A.M. Mr. T. G. I. James: Spinal Cord Tumours.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY
3.30 P.M. Mr. N. Asherson: Deafness.
5.30 P.M. Mr. G. H. Howells: Malignant Diseases of the Accessory Sinuses.

For infections of...



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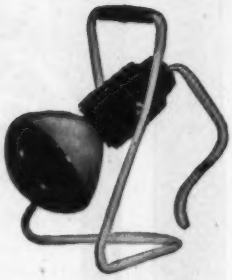

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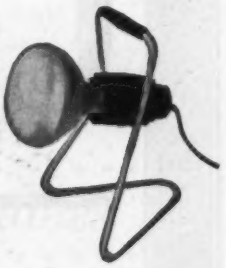

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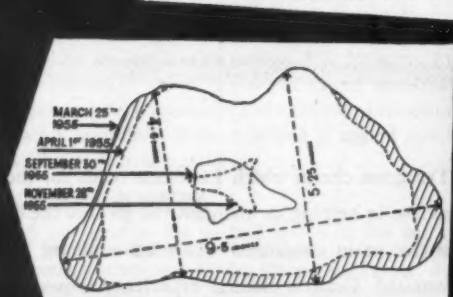

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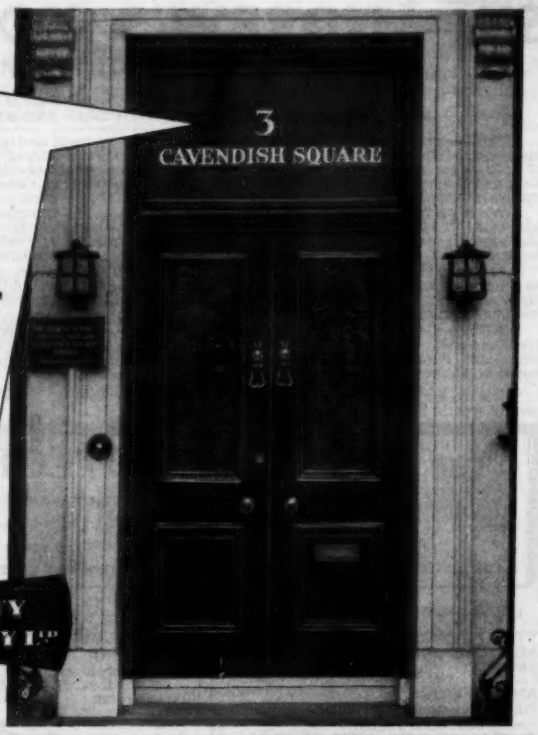

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The Terms and Conditions of Service of Hospital Medical and Dental Staff apply to all N.H.S. hospital posts we advertise, unless otherwise stated. Canvassing disqualifies, but candidates may normally visit the hospital by appointment.

Academic and Educational

THE ROYAL SOCIETY

ROYAL SOCIETY RESEARCH FELLOWSHIP

Applications are invited by the Council of the Royal Society for a Royal Society Research Fellowship in Cytology, and/or Cyto-chemistry with special reference to malignant cells. The Fellowship is tenable in any university, hospital, or medical school in the United Kingdom or at any other place approved by the Council of the Royal Society.

The appointment falls into the category of the Society's research fellowships which are intended for younger persons. It will be 2 years in the first instance, from 1st October, 1958, or a date to be arranged, and may be renewed annually up to a total of 5 years. It will be subject to the conditions governing Royal Society Research Appointments. The stipend will be in the range £1450 to £1850 p.a., depending upon qualifications. There will be superannuation benefits to which the successful candidate will be required to contribute 5% of annual stipend and to which the Society will contribute a sum equivalent to 10% of the annual stipend. Children's allowances are payable.

Applications should be made on forms to be obtained from the Assistant Secretary, The Royal Society, Burlington House, London, W.1, and should be received not later than 15th February, 1958.

November, 1957.

MEDICAL RESEARCH COUNCIL

FELLOWSHIPS IN CLINICAL RESEARCH

The Medical Research Council invite applications for Fellowships in Clinical Research, tenable at centres in the United Kingdom during the academic year 1958–59. These Fellowships are open to suitably qualified medical graduates who desire to prepare themselves for a career in clinical research. In general, it is intended that each Fellow appointed under the scheme should be given an opportunity, as part of his training for clinical research, to study methods of research in the basic subject most relevant to his particular clinical interest.

The awards will be made for a period of 1 year in the first instance and will be renewable annually in approved cases up to a maximum of 3 years in all. Stipend will be at the rate of £950 p.a., rising by annual increments of £75 to £1100 p.a., with superannuation provision in addition.

Candidates for these Fellowships, which are ordinarily restricted to British subjects resident in the United Kingdom, must be medically qualified and clinically experienced, and should preferably have worked for a period in a department in which clinical research was in progress. Applicants will be invited to submit their own proposals as to type and place of work, but the Council will be glad to advise successful candidates on the selection of suitable centres of study and to assist in placing them in departments or laboratories where the desired training and experience can be obtained.

Applications must be sponsored in each case by the head of the appropriate department in the candidate's University or Medical School, and an undertaking will be required that a suitable academic post in a clinical department will be available to the candidate in that institution on satisfactory completion of the period of study under the Fellowship.

Forms of application for these Fellowships may be obtained from the Secretary, Medical Research Council, 38, Old Queen-street, London, S.W.1, with whom applications should be lodged as soon as possible, and in any event not later than 1st March, 1958.

POSTGRADUATE LECTURES AT ST. MARK'S HOSPITAL

(in association with the British Postgraduate Medical Federation)

During MARCH, 1958, a series of 5 LECTURE-DEMONSTRATIONS will be given at St. Mark's Hospital on Saturday mornings from 9.30 to 12. These are intended as a revision course in surgical diseases of the rectum and colon for postgraduate students working for the F.R.C.S.

Date 1958	*Subjects*
1st March ..	The Anatomy and Physiology of the Rectum and Colon, Hæmorrhoids, Fissure and Fistula.
8th " ..	Cancer of the Rectum and Anus.
15th " ..	Cancer of the Colon: Polyps and Polyposis.
22nd " ..	Ulcerative Colitis.
29th " ..	Diverticulitis: Rectal Prolapse.

At least 2 of the members of the staff of St. Mark's Hospital will be present on each occasion to take part in the teaching.

Not more than 20 students will be accepted.

The fee for the whole 5-week course will be 5 guineas.

Application for admission should be made to the Dean, Dr. CUTHBERT DUKES, at St. Mark's Hospital, City-road, London, E.C.1.

INSTITUTE OF DERMATOLOGY

ST. JOHN'S HOSPITAL FOR DISEASES OF THE SKIN
Lisle-street, London, W.C.2

SHORT COURSES IN HISTOPATHOLOGY AND MEDICAL MYCOLOGY MARCH, 1958

Histopathology of the Skin: 5-day course will commence on 24TH MARCH, 1958. Fee 5 guineas.

Medical Mycology: 3½-day course will commence on 31ST MARCH, 1958. Fee 3 guineas.

Both courses are designed primarily for Clinical Pathologists but others may attend by arrangement.

Applicants should indicate their professional status to the Director of Pathology.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE

A 5-month DIPLOMA IN INDUSTRIAL HEALTH COURSE will commence on 7TH FEBRUARY, 1958, leading to the D.I.H. Examination of the Society of Apothecaries in London in July, 1958.

Applications to The Dean, 23, Queen-square, W.C.1.

UNIVERSITY OF MANCHESTER

DIPLOMA IN BACTERIOLOGY

The COURSE for the Diploma in Bacteriology requires full-time attendance in the Department of Bacteriology for 1 academic year (October–June). It is suitable for these who have qualified in medicine, veterinary medicine or other branches of science related to bacteriology. The course includes general and systematic bacteriology, bacterial chemistry, serology, immunology, virology, mycology and statistics.

All candidates must present evidence of previous training approved by Senate as satisfactory for admission to the course and register as postgraduate students of the University.

Further particulars and forms of application may be obtained from the Secretary, Department of Bacteriology, York-place, Manchester, 13.

ROYAL FREE HOSPITAL. Applications are invited for 3 ASSISTANTS in the Department of Pathology. The successful candidates will be required to work under the direction of the Professor of Pathology and assist in the routine work in morbid anatomy, and also assist in a research project, either on liver or ischæmic heart disease. The appointment will be made for 1 year in the first instance, commencing 1st April, 1958, and preference will be given to candidates with a postgraduate degree and previous experience in pathology; these latter 2 qualifications are not essential, and the appointment can be considered as a training post. Salary will be £935 p.a. and will carry superannuation.

Applications should be sent to the Professor of Pathology, Royal Free Hospital, Gray's Inn-road, London, W.C.1, with the names of 2 referees, before 1st March, 1958.

UNIVERSITY OF LONDON. Application is invited for the MARY SCHARLIEB RESEARCH STUDENTSHIP, of the value of £250 for 1 year in the first instance. The Studentship is open to graduates of the University who are registered medical practitioners or possess other qualifications which, in the opinion of the Senate, would enable them to undertake postgraduate medical research.

Application (on prescribed form) must reach the Secretary to the Scholarships Committee, Senate House, London, W.C.1 (from whom forms and further particulars may be obtained), not later than 28th February, 1958.

UNIVERSITY OF LONDON. The Senate invite applications for the READERSHIP IN MEDICINE, tenable at St. Bartholomew's Hospital Medical College (salary £2050–£100–£2550 a year).

Applications (10 copies) must be received not later than 17th February, 1958, by the Academic Registrar, University of London, Senate House, W.C.1, from whom further particulars may be obtained.

AUSTRALIA. UNIVERSITY OF QUEENSLAND. Applications are invited for the position of LECTURER IN RADIATION PHYSICS. Applicants should have a degree (preferably an honours degree) with physics as major subject and preference will be given to an applicant with experience in hospital physics. Salary £A1300–£A1750 p.a.

Further particulars are obtainable from the Secretary, Association of Universities of the British Commonwealth, 36, Gordon-square, London, W.C.1. Applications close, in Australia and London, on 15th February, 1958.

AUSTRALIA. UNIVERSITY OF SYDNEY. Applications are invited for the position of LECTURER IN MEDICINE. Salary for a Lecturer is within the range £A1200–£80–£1750 p.a., plus cost-of-living adjustment and will be subject to deductions under the State Superannuation Act. The commencing salary will be fixed according to the qualifications and experience of the successful applicant. (The current scale of salaries is under revision.) Under the Staff Members' Housing Scheme in cases approved by the University and its Bankers, married men may be assisted by loans to purchase a house.

Further particulars and information as to the method of application may be obtained from the Secretary, Association of Universities of the British Commonwealth, 36, Gordon-square, London, W.C.1. The closing date for the receipt of applications, in Australia and London, is 28th February, 1958.

UNIVERSITY OF BRITISH COLUMBIA, Vancouver 8, B.C., CANADA, requires a Full-time STAFF MEMBER in Preventive Medicine in the Faculty of Medicine. Applicants should be graduates in medicine with interest in epidemiological investigation. Salary and academic rank commensurate with training and experience.

Address inquiries to Dr. JAMES M. MATHER, Professor of Public Health.

Hospital Services: Senior Appointments

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) at Tooting Bec Hospital, S.W.17 (2100 Beds). The Hospital has observation ward beds, Outpatient Department, and a non-statutory unit, in addition to a large geriatric section. Experience of modern methods of treatment essential and candidates should possess D.P.M. Accommodation available, if required, for a single officer.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 8th February, 1958. Applicants may visit hospital by local arrangement.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD.

1. CONSULTANT PHYSICIAN in Physical Medicine, 2 half-days a week, Acton Hospital, Gunnersbury-lane, W.3 (84 Beds).

Applications before 17th February, 1958.

2. CONSULTANT ANÆSTHETIST, whole-time or maximum sessions, Edgware General Hospital, Edgware, Middlesex (638 Beds). Duties will include emergencies at Bushey Maternity Hospital (50 obstetric beds).

Applications before 24th February, 1958.

3. CONSULTANT ORTHOPÆDIC SURGEON, 2 half-days a week, St. Charles' Hospital, Ladbroke-grove, W.10 (575 Beds).

Applications before 26th February, 1958.

Hospitals may be visited by direct appointment.

Application forms obtainable from and returnable to Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1.

ST. THOMAS'S HOSPITAL, London, S.E.1. Physician to the Pædiatric Department. Consultant status, with membership of the Medical Committee. 4 sessions per week. Vacant 13th October, 1958.

Applications (12 copies), naming 3 referees, to Clerk of the Governors by 14th February, 1958.

ST. THOMAS'S HOSPITAL, London, S.E.1. Anæsthetist. Consultant status, with membership of the Medical Committee. 6 sessions per week. Vacant 12th November, 1958.

Applications (12 copies), naming 3 referees, to Clerk of the Governors by 14th February, 1958.

COLCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited for post of Locum CONSULTANT RADIODIAGNOSTICIAN based on Essex County Hospital, Colchester, for the period 28th June–17th August, 1958.

Applications, with copies of 3 testimonials, to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester.

HASTINGS HOSPITAL MANAGEMENT COMMITTEE. Locum CONSULTANT ANÆSTHETIST required for 9 sessions weekly as from 17th February, 1958, for a period of not less than 7 weeks.

Apply in writing to the Group Secretary, 11, Holmesdale-gardens, Hastings, together with copies of current testimonials or names of 2 referees, by not later than 31st January, 1958.

LEEDS REGIONAL HOSPITAL BOARD

CONSULTANT in Anæsthetics (maximum part-time sessions). Hospitals in the East Riding of Yorkshire—mainly at Westwood Hospital, Beverley. 1 session at Hull Royal Infirmary. Person appointed to reside in Beverley.

Whole-time ASSISTANT GERIATRICIAN (Senior Hospital Medical Officer scale) for duties at hospitals in the Leeds A and B Groups (933 Beds). The successful candidate will work under the Consultant Geriatrician, and will be required to reside in or near Leeds. There is an organised Area Geriatric Service in existence. The post offers good experience to candidates of Senior Registrar (or equivalent status) in general medicine who may decide to specialise in geriatrics, and there are excellent opportunities for gaining experience in rehabilitation and physical medicine.

Whole-time or Part-time ASSISTANT OPHTHALMOLOGIST/S (Senior Hospital Medical Officer scale) for duties at the Royal Eye and Ear Hospital, Bradford (3 sessions) and School Clinics at Bradford and the adjacent West Riding Areas (3 sessions), and Dewsbury (1 session). The Board is prepared to consider applications from suitably qualified and experienced practitioners either for whole-time or for part-time employment. Applicants for part-time work should state the maximum number of sessions which they can undertake.

Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer scale), Broadgate Hospital, Beverley, and associated clinics at Beverley, Driffield and Hull. Married accommodation may be available. Candidates should normally hold a D.P.M. but applications will also be considered from candidates without previous experience in psychiatry who hold a higher medical qualification, have had wide experience in general medicine in the Senior Registrar grade and intend to obtain a D.P.M. and specialise in psychiatry.

Applications (12 copies), stating age, qualifications and details of present and previous appointments with dates, and names and addresses of 3 referees, to The Secretary, Park-parade, Harrogate, by 11th February, 1958.

LIVERPOOL REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens ANÆSTHETIST (Consultant) required for approximately 6 months with duties mainly in the Southport and Ormskirk Groups.

Forms of application from Dr. T. LLOYD HUGHES, Senior Administrative Medical Officer, Liverpool Regional Hospital Board, 19, James-street, Liverpool, 2, to be returned not later than 1st February, 1958.

VINCENT COLLINGE, Secretary to the Board.

NORTH GLOUCESTERSHIRE CLINICAL AREA. South WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of ASSISTANT PSYCHIATRIST to Horton Road and Coney Hill Hospitals, Gloucester. These Hospitals are run on open door lines. The appointment, which becomes vacant on 1st July, 1958, will be on a whole-time basis in the Senior Hospital Medical Officer grade. The successful candidate will work under the general direction of the Medical Superintendent of Horton Road and Coney Hill Hospitals.

Applications (12 copies), stating date of birth, qualifications and experience, together with the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 3rd February, 1958.

SHEFFIELD REGIONAL HOSPITAL BOARD. Maximum Part-time CONSULTANT ANÆSTHETIST required for the City General Hospital and Wharncliffe Hospital, Sheffield.

Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by 17th February, 1958.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. Applications invited for the appointment of Whole-time ASSISTANT CHEMICAL PATHOLOGIST (salary in accordance with SENIOR HOSPITAL MEDICAL OFFICER scale) in the above Teaching Hospitals. Experience of general pathology and of chemistry is essential; a higher medical qualification is desirable, as is a scientific qualification.

Applications, with the names of 3 referees, to be sent to the Chief Administrative Officer, United Sheffield Hospitals, Weststreet, Sheffield, 1, not later than 8th February, 1958, from whom further details may be obtained.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as CONSULTANT in Diagnostic Radiology (whole-time or 9 notional half-day sessions a week) in the Isle of Thanet Group of hospitals. The post will be vacant from 13th June, 1958. Candidates must have had a wide experience in the specialty and hold an appropriate diploma. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales). Candidates may visit the hospitals concerned.

Apply, stating nationality, age, sex, qualifications and experience, including details of present appointment and of war service, together with the names and addresses of 3 referees, to the Secretary, Advisory Appointments Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 1st February, 1958.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for appointment as Part-time CONSULTANT ANÆSTHETIST to the St. Francis and The Lady Chichester Group of hospitals for duties at the Neuropsychiatric Unit at Hurstwood Park, Haywards Heath, Sussex, to cover neurosurgical operating sessions on Wednesdays (mornings and afternoons), and at other times to be arranged, together with emergencies. Either 1 or more appointments within a total of 4 notional half-days a week may be made. Candidates must be experienced anæsthetists, preferably with training and practice in anæsthetics for neurosurgery, and hold the appropriate qualifications. Applicants may visit the hospital.

Apply, stating nationality, age, sex, qualifications, experience and number of notional half-days for which available, including details of present appointment and of war service, together with the names and addresses of 3 referees, to the Secretary, Advisory Appointments Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 1st February, 1958.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires CONSULTANT RADIOLOGIST (whole-time or maximum part-time) for the St. Helier (Surrey) Group of hospitals. Duties mainly at St. Helier Hospital, Carshalton, although there will be work at other hospitals, including 2 sessions a week at Wilson Hospital, Mitcham. Applicants should have D.M.R., and wide experience in radiology; a special interest, or higher qualification, would be an advantage.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 15th February, 1958. Applicants may visit hospitals by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time CONSULTANT PSYCHIATRIST at Cane Hill Hospital, Coulsdon, Surrey. There are at present some 2300 patients resident and 4 outpatient clinics; the Hospital undertakes postgraduate teaching in association with the Institute of Psychiatry. Candidates should possess the D.P.M. and a higher medical qualification and should preferably have had experience in a senior position at a progressive mental hospital. An unfurnished maisonette (7 rooms, with garden) is available.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary, (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 15th February, 1958. Applicants may visit hospital by arrangement with Physician-Superintendent.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time CONSULTANT PSYCHIATRIST at Knowle Hospital, Fareham, Hants. Candidates should possess D.P.M. and a higher medical qualification, and should have had wide experience of mental hospital psychiatry.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 15th February, 1958. Applicants may visit hospital by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade) at Warlingham Park Hospital, Warlingham, Surrey. Candidates should possess D.P.M. and have wide experience in psychiatry. Training and experience in child psychiatry an advantage. Hospital uses all modern psychiatric treatments and emphasises occupational, social and group methods. Single accommodation available if required.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 8th February, 1958. Applicants may visit hospital by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Part-time CONSULTANT PHYSICIAN (7 half-days per week) for the Guildford (Surrey) Group of hospitals. Duties mainly at St. Luke's Hospital, Guildford. Successful candidate will be expected to live in or near Guildford.

Applications by letter (5 copies), giving date of birth, qualifications, experience, and names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 15th February, 1958. Applicants may visit hospital(s) by local arrangement.

SCOTLAND. NORTH-EASTERN REGIONAL HOSPITAL BOARD requires a Whole-time CONSULTANT BACTERIOLOGIST to take charge of the Laboratory at the City Hospital, Aberdeen. The Laboratory undertakes Public Health work and Hospital work and the examination of specimens referred by general practitioners from the whole of the north-eastern area of Scotland.

Applications, together with the names of 2 referees, should be forwarded by 1st February, 1958, to the Senior Administrative Medical Officer, 1, Albyn-place, Aberdeen, from whom further particulars and a form of application may be obtained.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Whole-time PSYCHIATRIST (Senior Hospital Medical Officer grade) at East Lothian Mental Hospital, Haddington (235 Beds). The successful candidate will be expected to take an active part in the development of the outpatient and other psychiatric services in the area.

Apply, giving particulars of age, qualifications and previous experience, and the names of 3 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, within 30 days.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of Whole-time ASSISTANT RADIOLOGIST based at the Dumfries and Galloway Royal Infirmary, Dumfries. Salary (at age 32 and over) on the scale £1653 15s.–£52 10s.–£2126 5s.

Applications (16 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, not later than 30 days after the publication of this advertisement.

VANCOUVER, CANADA. BRITISH COLUMBIA CANCER INSTITUTE. 2 RADIOTHERAPISTS required. Salary range, $10,000–$16,000 p.a. depending on experience.

Applicants may write or interview Dr. A. M. EVANS at the Dorchester Hotel, Park-lane, London, from 8th January to 25th January, 1958.

SOUTH AFRICAN BLOOD TRANSFUSION SERVICE. SEROLOGIST. Applications are invited from registered medical practitioners with experience in clinical pathology. Salary scale £1700–£100–£2400; commencing notch according to experience. Annual leave 42 days, of which 21 days may be accumulated to a maximum of 6 months; also annual leave allowance equivalent to 5% of annual salary rising to 10% after 10 years' service. Membership of Staff Provident Fund compulsory after confirmation of appointment to permanent staff, contributions being 7½% of salary by the Service and 5% by the employee. The appointment will be on a probationary basis for the first 6 months.

Further particulars may be obtained on application to the Secretary, South African Blood Transfusion Service, P.O. Box 9326, Johannesburg.

Hospital Services: Junior Appointments

ACTON HOSPITAL, Gunnersbury-lane, Acton, W.3. SENIOR HOUSE OFFICER (resident) required as Casualty Officer from 7th January, 1958. Ministry of Health conditions of service.

Applications, with copies of 2 testimonials, to Hospital Secretary within 7 days.

BATTERSEA GENERAL HOSPITAL, Battersea Park, S.W.11. HOUSE SURGEON/CASUALTY OFFICER. Combined Post. Resident. Vacant early February. House Officer grade, not pre-registration and not recognised for F.R.C.S.

Apply, enclosing copies of 2 recent testimonials, to Hospital Secretary, with whom arrangements can be made to view the Hospital.

BETHLEM ROYAL HOSPITAL AND THE MAUDSLEY HOSPITAL. Applications are invited from registered medical practitioners for the appointment of REGISTRAR for the period from 1st April, 1958, to 7th April, 1959, at the above Postgraduate Teaching Hospital, with which is associated the Institute of Psychiatry (University of London). Candidates with experience in general medicine and neurology or in psychology will receive special consideration.

Applications, giving details of experience and the names of 2 referees, should be made within 2 weeks of the appearance of this advertisement. Application forms obtainable from K. J. JOHNSON, House Governor and Secretary, Maudsley Hospital, Denmark Hill, London, S.E.5.

BETHLEM ROYAL HOSPITAL AND THE MAUDSLEY HOSPITAL. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER for the period from 1st April, 1958, to 7th April, 1959, at the above Postgraduate Teaching Hospital, with which is associated the Institute of Psychiatry (University of London). Experience in general medicine and neurology or in the basic sciences is an advantage.

Applications, giving details of experience and the names of 2 referees, should be made within 2 weeks of the appearance of this advertisement. Application forms obtainable from K. J. JOHNSON, House Governor and Secretary, Maudsley Hospital, Denmark Hill, London, S.E.5.

BETHNAL GREEN HOSPITAL, Cambridge Heath-road, E.2. Applications are invited for the pre-registration post of HOUSE PHYSICIAN vacant 13th February, 1958.

Applications, stating experience, and copies of 2 testimonials, to Hospital Secretary.

CONNAUGHT HOSPITAL, Walthamstow, E.17. (123 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST, graded Senior House Officer. Post vacant 16th February, 1958. Salary £819 10s. p.a., less £150 p.a. for board, lodging, &c. Recognised for D.A. and F.F.A. R.C.S.

Applications, stating age, qualifications and experience, together with copies of 2 recent testimonials, should be sent immediately to Secretary, Hospital Management Committee, Forest Group, Langthorne-road, E.11.

CHILDREN'S HOSPITAL, Sydenham, S.E.26. House OFFICER (medicine and surgery) required 1st March. Recognised for D.C.H.

Apply, naming 2 referees, to Administrative Officer by 24th January.

DREADNOUGHT SEAMEN'S HOSPITAL, Greenwich, S.E.10. HOUSE SURGEON (pre-registration) required on 13th February.

Applications, stating age, nationality, qualifications and experience, and giving the names of 3 recent referees, should be sent to the Secretary at the above address not later than 25th January.

ELIZABETH GARRETT ANDERSON HOSPITAL, Euston-road, N.W.1. (ROYAL FREE HOSPITAL GROUP.) Applications are invited from pre-registration and registered Women medical practitioners for the post of HOUSE SURGEON to Gynæcological Department (recognised for M.R.C.O.G.). Duties to commence 1st March, 1958. Appointment for 6 months. Salary in accordance with Ministry of Health scale for House Officers.

Applications, with copies of 3 recent testimonials, should be sent to the Secretary, Elizabeth Garrett Anderson Hospital, by 28th January, 1958.

FULHAM HOSPITAL, St. Dunstan's-road, Hammersmith, W.6. Applications are invited for appointment as SURGICAL REGISTRAR. Post vacant 1st March, 1958. Candidates may visit the Hospital by arrangement with the Surgeon-Superintendent.

Applications (5 copies) to be submitted immediately, on forms obtainable from, and returnable to, Group Secretary (L.123), 5, Collingham-gardens, London, S.W.5.

GERMAN HOSPITAL, London, E.8. (General—157 Beds.) Applications for the 6-month resident post, vacant 4th February, of Pre-registration HOUSE SURGEON should reach the Group Secretary, Hackney Hospital, London, E.9, by 27th January, quoting GH/PHS.

GUY'S HOSPITAL AND THE SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited to fill the established vacancy for a SENIOR REGISTRAR in Diagnostic Radiology to the Board of Governors of Guy's Hospital and the South East Metropolitan Regional Hospital Board, in the Bromley Group, on an exchange basis during a 4-year tenure of the post. The appointment will be made jointly by the bodies concerned. The post, which will be reviewed annually, is subject to the terms and conditions of service of hospital medical and dental staff (England and Wales) with duties commencing on 1st March, 1958.

Forms of application are obtainable from, and should be lodged with, the Superintendent, Guy's Hospital, London Bridge, S.E.1, not later than 25th January, 1958.

HACKNEY HOSPITAL, London, E.9. (General, 841 Beds.) Applications for the 6-month resident post, vacant end of February, of Pre-registration HOUSE PHYSICIAN should reach Secretary, above address, by 3rd February, quoting HH/PHP.

HAMMERSMITH HOSPITAL AND INSTITUTE OF OBSTETRICS AND GYNÆCOLOGY AND SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Joint appointment. Whole-time REGISTRAR (obstetrics and gynæcology) required 1st April. Appointment tenable for 2 years, the first 6 months at Hammersmith Hospital and Institute of Obstetrics and Gynæcology, the next year at the Brighton and Lewes Group of hospitals, returning to Hammersmith Hospital for the final 6 months.

Applications, stating age, qualifications, experience, names of 2 referees, to Secretary, The Board of Governors of the Hammersmith, West London and St. Mark's Hospitals, Ducane-road, London, W.12, by 1st February, 1958.

KING EDWARD MEMORIAL HOSPITAL, Ealing, W.13. HOUSE OFFICER in Gynæcology at above Hospital, with opportunity for a little obstetrics at Perivale Maternity Hospital, Greenford. Pre-registration surgical post. Preference given to persons seeking second pre-registration post under the Medical Act, 1950.

Applications, stating age, nationality, qualifications and experience, with copies of 2 recent testimonials, to Group Secretary, South West Middlesex Hospital Management Committee, West Middlesex Hospital, Isleworth, by 27th January.

LAMBETH HOSPITAL, Brook-drive, S.E.11. Applications are invited from pre-registration and registered medical practitioners for the appointment of RESIDENT HOUSE SURGEON in the Obstetric and Gynæcological Unit. Appointment for 6 months from 1st March, 1958. Convenient if successful candidate could carry out a fortnight's locum duty from 15th February, 1958. Hospital recognised for M.R.C.O.G. and D.Obst.R.C.O.G.

Application forms from the Secretary. Self addressed envelope should be enclosed.

LONDON CHEST HOSPITAL (Country Branch). HOSPITALS FOR DISEASES OF THE CHEST. REGISTRAR in Clinical Pathology (Registrar grade). A vacancy occurs at the country branch near Letchworth. The appointment is a whole-time one and will be for 1 year in the first instance and the holder may be resident or non-resident.

Applications, stating age, qualifications with dates, and previous experience, together with copies of 3 testimonials, should reach the undersigned not later than 22nd January, 1958.

G. BRATT, Acting House Governor.

London Chest Hospital, E.2.

NORTH MIDDLESEX HOSPITAL AND EDMONTON CHEST CLINIC, London, N.18. Applications are invited for the post of SENIOR HOUSE OFFICER (tuberculosis), resident, for 1st March. Appointment for 6 months in the first instance with possible extension to 1 year. Duties at above Hospital and Clinic under direction of the Chest Physician. Further details on request.

Applications, stating age, qualifications, experience, with copies of recent testimonials and/or names of 2 referees, to Hospital Secretary, by 30th January.

NORTH MIDDLESEX HOSPITAL, London, N.18. 2 RESIDENT HOUSE PHYSICIANS required, for 1st March, for 6 months. General medicine. Approved pre-registration posts (first or second).

Applications (in own handwriting), stating age, nationality, qualifications, experience, with copies of recent testimonials, to Hospital Secretary, by 29th January.

PADDINGTON GENERAL HOSPITAL, Harrow-road, W.9. (582 Beds.) Applications are invited for the post of REGISTRAR (surgical) whole-time, non-resident. Experience includes general ward and outpatient work, and the supervision and teaching of medical students from St. Mary's Hospital Medical School. The Hospital may be visited by direct appointment.

Application forms obtainable from and returnable to the Secretary to the Committee, Paddington Group Hospital Management Committee, Harrow-road, W.9, by 29th January, 1958.

POPLAR HOSPITAL, East India Dock-road, E.14. Senior HOUSE OFFICERS (2) required at above Hospital. Duties are mainly in connection with the receiving room and Casualty Departments. 1 post vacant now, the other post vacant end of February.

Applications, giving full details, to Group Secretary, Bow Group Hospital Management Committee, 2A, Bow-road, E.3.

QUEEN CHARLOTTE'S AND CHELSEA HOSPITALS. CHELSEA HOSPITAL FOR WOMEN, Department of Pathology. Applications are invited for the post of REGISTRAR in Pathology. Previous experience is desirable and details of the post can be obtained from the Director of the Department. The post is non-resident.

Applications to the House Governor by 31st January, on forms obtainable from 339, Goldhawk-road, London, W.6.

QUEEN CHARLOTTE'S AND CHELSEA HOSPITALS. QUEEN CHARLOTTE'S MATERNITY HOSPITAL. SENIOR HOUSE OFFICER in the Pædiatric Department. Resident post tenable for 6 months in the first instance from 1st April, 1958. Duties will include the supervision of the babies, research work under the visiting staff, and charge of the follow-up clinics. Previous experience at a children's hospital is essential and possession of a higher qualification is desirable.

Applications to the House Governor by 27th January, 1958, on forms obtainable from 339, Goldhawk-road, London, W.6.

QUEEN MARY'S HOSPITAL, Roehampton, London, S.W.15. (348 Beds.) SURGICAL REGISTRAR required whole time. National Health Service terms and conditions.

Detailed applications (4 copies), giving nationality, date of birth, qualifications, experience, present appointments and names of 3 referees, should reach the Secretary, Ministry of Health, Division 4(v), Norcross, Blackpool, Lancs, by 8th February, 1958.

QUEEN MARY'S HOSPITAL FOR THE EAST END, STRATFORD, E.15. HOUSE PHYSICIAN (third post) for 6 months commencing 18th February, 1958.

Applications, with the names of 2 referees, to Hospital Secretary by 25th January, 1958.

REGIONAL NEUROSURGICAL CENTRE (66 Beds), BROOK GENERAL HOSPITAL, Shooters Hill-road, S.E.18. SENIOR HOUSE OFFICER (neurosurgery). Vacant early February. Post recognised for F.R.C.S. and D.P.M. and provides excellent opportunity for training in neurology.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

ROYAL LONDON HOMŒOPATHIC HOSPITAL, Great Ormond-street and Queen-square, W.C.1. Applications are invited from registered medical practitioners for the post of RESIDENT HOUSE SURGEON with care of gynecological beds. Vacant 10th February, 1958. Post tenable for 6 months. Candidates will be required to attend for interview.

Applications, stating age and full particulars, to Secretary.

ROYAL NATIONAL THROAT, NOSE AND EAR HOSPITAL, Gray's Inn-road, W.C.1, and Golden-square, W.1, with which is associated the Institute of Laryngology and Otology (University of London). GENERAL PRACTITIONER CLINICAL ASSISTANTS and OUTPATIENT ASSISTANTS. These appointments give those engaged in general practice who are able to attend for 2 sessions weekly over a period of 15 months commencing in March, 1958, the opportunity of widening their clinical experience in the specialty. At the end of 3 months' training period the holders will be appointed as Outpatient Assistants with remuneration under paragraph 10 (b) of the National Health Service terms and conditions of service.

Further particulars may be obtained from the House Governor.

SOUTH EAST REGIONAL THORACIC SURGERY UNIT (50 Beds), BROOK GENERAL HOSPITAL, Shooters Hill-road, S.E.18. SENIOR HOUSE OFFICER. Vacant mid-February. Recognised for F.R.C.S. 6 months' appointment and may then be renewed for a further period. The Unit treats all types of chest diseases and offers opportunity for comprehensive training in thoracic surgery.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

SOUTH WESTERN HOSPITAL, Landor-road, S.W.9. Applications are invited from Women candidates for the post of HOUSE SURGEON (pre-registration) at the above Hospital. Vacant 1st February, 1958. Duties include general surgery and the successful candidate will also be required to relieve the House Surgeon at the Annie McCall Maternity Hospital.

Application forms from the Hospital Secretary to be returned as soon as possible.

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN, Clapham Common, S.W.4. Applications are invited from registered medical Women for the post of SENIOR HOUSE OFFICER in Pathology. Vacant 24th March, 1958. Previous experience in laboratory work is not essential. Applicants will be required to live near the Hospital.

For forms of application apply to the Secretary.

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN, Clapham Common, S.W.4. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited from Women medical practitioners for the post of MEDICAL REGISTRAR (7 sessions weekly), vacant 1st April, 1958. The appointment will be for 1 year in the first instance. Canvassing will disqualify but candidates are not precluded from visiting the Hospital.

For forms of application apply (enclosing self-addressed envelope) to the Secretary, Lambeth Group Hospital Management Committee, Renfrew-road, S.E.11, to whom completed forms should be returned not later than 1st February, 1958.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Anæsthetics to fill a vacancy in the approved trainee establishment at the Bermondsey and Southwark Group of hospitals. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 1st February, 1958.

ST. ANN'S GENERAL HOSPITAL, N.15. Applications are invited from registered medical practitioners for the appointment of RESIDENT HOUSE SURGEON (Senior House Officer) to above Hospital for a period of 6 months from 9th February, 1958.

Application form from Secretary, Tottenham Group Hospital Management Committee, The Green, N.15, to be returned by 31st January, 1958.

ST. CLEMENT'S HOSPITAL, Bow, E.3. House Physician (not pre-registration) for general medical wards.

Applications, stating age, qualifications and experience, together with the names and addresses of 2 referees, to be sent to Hospital Secretary immediately.

ST. JAMES' HOSPITAL, Balham, London, S.W.12. Senior HOUSE OFFICER (gynæcology). Post vacant 1st March. Recognised for M.R.C.O.G.

Applications, stating age, qualifications, experience and names of 2 referees, to Group Secretary, Wandsworth Hospital Group, at above address by 31st January.

ST. JAMES' HOSPITAL, Balham, London, S.W.12. House PHYSICIAN (pædiatric) required 1st March. Post recognised for D.C.H. Successful candidate will also be required to assist in Department of Pathology.

Applications, stating age, qualifications, experience, and names of 2 referees, to Group Secretary, Wandsworth Hospital Group, at above address by 29th January.

ST. MARK'S HOSPITAL, City-road, London, E.C.1. Applications invited from Senior Registrars who have completed their training or Registrars who have completed their appointments for the post of RESIDENT SURGICAL OFFICER. Part of time non-resident by arrangement. Salary at the rate of £1540 or £1061 10s. respectively. Appointment tenable for 6 months from 1st April with possibility further extension 6 months.

Applications, stating age, qualifications, experience, names 2 referees, to Secretary, The Board of Governors, The Hammersmith, West London and St. Mark's Hospitals, Ducane-road, London, W.12, by 1st February.

ST. MARY'S HOSPITAL, Children's Department, PRINCESS LOUISE KENSINGTON HOSPITAL FOR CHILDREN, St. Quintin-avenue, London, W.10. HOUSE OFFICERS (2) required (second or third post). Pre-registration candidates considered. Vacant 1st March, 1958.

(*a*) Mainly medical.
(*b*) E.N.T. and casualty.

Recognised for the D.C.H.

Applications, with names of 2 referees, to the undersigned not later than 27th January, 1958.

A. C. YOUNG, Secretary.

ST. MARY'S HOSPITAL, Paddington, W.2. Applications are invited from suitably qualified Male candidates for the post of Whole-time REGISTRAR in the Venereal Diseases Department. The appointment, which is eminently suitable for persons reading for a higher qualification, is for a first period of 12 months as from 1st March, 1958, the holder being eligible for re-election.

Applications, stating nationality, date of birth, qualifications, details of experience, together with dates and National Health Service gradings of previous and present appointments and name and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 3rd February, 1958.

ST. MARY'S HOSPITAL, Paddington, W.2. Registrar (whole-time) required to the Allergy Clinics (Wright Fleming Institute of Microbiology). The appointment is for a first period of 12 months with effect from 4th March, 1958; remuneration to be at "Registrar" rates.

Applications, stating nationality, date of birth, permanent address, qualifications with dates and details of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 28th January, 1958.

ST. MARY'S HOSPITAL, Paddington, W.2. 2 Casualty SURGEONS (non-resident) required for a first period of 6 months with effect from 1st March, 1958. Remuneration to be at "Senior House Officer" rates. Candidates must have held an appointment as House Surgeon at this Hospital or at another Hospital approved by the Board of Governors.

Applications, stating nationality, date of birth, permanent address, qualifications with dates, and details of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 28th January, 1958.

ST. MARY'S HOSPITAL, Paddington, W.2. Outpatient SURGICAL ASSISTANT (part-time, graded Senior House Officer) required for 3 notional half-days per week. The appointment, which is for a first period of 12 months, is designed for men or women who have already passed their Primary F.R.C.S., and is ideally suited for those reading for the Final, as a large number of clinical cases are available. The successful candidate will be required to take up duties as soon as possible.

Applications, stating nationality, date of birth, permanent address, qualifications with dates, and details of previous and present appointments, together with the names and addresses of 3 referees, should reach ALAN POWDITCH, House Governor, not later than 3rd February, 1958.

ST. PETER'S, ST. PAUL'S AND ST. PHILIP'S HOSPITALS. RESIDENT SURGICAL OFFICER (Senior Registrar grade) required for St. Peter's Hospital on 1st April, 1958. Applications invited from Male candidates on the British Register who have completed their training in general surgery. Appointment for 6 months, with opportunity for a further 6 months if recommended. Candidate should be prepared to spend 1 year at the hospital if required.

Applications (12 copies), and the names of 3 referees, should reach the House Governor, St. Peter's Hospital, Henrietta-street, W.C.2, by 1st February, 1958.

ST. STEPHEN'S HOSPITAL, Chelsea, S.W.10. Obstetric AND GYNÆCOLOGICAL HOUSE SURGEON (resident). Post-registration. Post recognised for D.Obst.R.C.O.G. Vacancy 18th February.

Applications, naming 2 referees, to Medical Superintendent within 14 days of date of advertisement.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy on 8th April, 1958, for a RESIDENT DENTAL HOUSE SURGEON (Senior House Officer). The post is recognised for the Fellowship in Dental Surgery, Royal College of Surgeons. Experience is given in both oral surgery and orthodontics.

Full particulars and form of application, which must be returned not later than Monday, 3rd February, 1958, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy on or about 18th April, 1958, for a SURGICAL OUTPATIENT ASSISTANT (Senior Registrar grade) for 1 session per week (Monday mornings).

Full particulars and form of application, which must be returned not later than Monday, 3rd February, 1958, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be vacancies on 15th April, 1958, for the following Senior House Officers:—

2 HOUSE PHYSICIANS.
1 HOUSE SURGEON.

Full particulars and form of application, which must be returned not later than Monday, 3rd February, 1958, may be obtained from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

UNIVERSITY COLLEGE HOSPITAL, Gower-street, W.C.1. Applications are invited for the post of MEDICAL REGISTRAR for 1 year in the first instance from 1st March, 1958. This post will include a period of duty at the Whittington Hospital, N.19. Preference will be given to candidates holding higher qualifications.

Applications, with names of 2 referees, to T. F. W. MACKEOWN, Administrator and Secretary, by 31st January, 1958.

WANSTEAD HOSPITAL, Hermon Hill, E.11. (191 Beds.) HOUSE SURGEON required. Recognised for F.R.C.S.

Applications, with full details and copies of 2 recent testimonials, should be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

WHIPPS CROSS HOSPITAL, Leytonstone, E.11. Applications are invited for the post of Pre-registration HOUSE SURGEON (orthopædics) which becomes vacant 4th March, 1958.

Application forms from the Hospital Secretary to be returned by 28th January, 1958.

WHIPPS CROSS HOSPITAL, Leytonstone, E.11. Applications are invited for the post of pre-registration HOUSE PHYSICIAN (general medicine) which becomes vacant 1st March, 1958.

Application forms from the Hospital Secretary to be returned by 28th January, 1958.

WHITTINGTON HOSPITAL, London, N.19. Medical REGISTRAR (Neurological and General). Vacant 1st April, 1958. Unit contains 60 Beds and is associated with the neuro-surgical unit. Post recognised for M.D. (London). Hospital may be visited by direct appointment.

Application forms obtainable from and returnable to Group Secretary, 46, Cholmeley Park, Highgate, N.6, by 27th January, 1958.

ABBOTS LANGLEY, HERTFORDSHIRE. LEAVESDEN HOSPITAL. Vacancy for JUNIOR HOSPITAL MEDICAL OFFICER, tenable for short term (2–3 years), at above Hospital, accommodating all grades of mentally defective patients. Recognised for D.P.M. 2 sanatoria for pulmonary tuberculosis. Geriatric hospital within the Group. Visited by specialists in a number of specialties.

Applications to Physician-Superintendent, Leavesden Hospital, Abbots Langley, Herts.

ALTRINCHAM GENERAL HOSPITAL. St. Anne's E.N.T. DEPARTMENT, ALTRINCHAM, CHESHIRE. (53 Beds.) REGISTRAR required (preferably resident). Vacant January, 1958. This post offers excellent opportunities of practical experience and is recognised under F.R.C.S. regulations.

Applications to be forwarded, with names of 2 referees, to the Group Secretary, North and Mid-Cheshire Hospital Management Committee, The Hospital, Sinderland-road, Altrincham, Cheshire.

ALEXANDRIA, DUNBARTONSHIRE. VALE OF LEVEN HOSPITAL. (156 Beds.) SENIOR HOUSE OFFICER required in Surgery and Gynæcology.

Applications should be submitted direct to the Medical Superintendent at the Hospital.

ASHFORD HOSPITAL, Ashford, Middlesex. (500 Beds.) STAINES GROUP HOSPITAL MANAGEMENT COMMITTEE. Required, RESIDENT HOUSE SURGEON for general surgical duties. 6 months' appointment, preference given to pre-registration candidates.

Applications, stating age, qualifications and experience, with copies of up to 3 recent testimonials, to Medical Director of Hospital immediately.

BARNSTAPLE. NORTH DEVON INFIRMARY. (105 Beds.) HOUSE SURGEON (pre-registration); vacant now. The Hospital serves a wide area of pleasant countryside and the post affords good opportunity to study excellent clinical material.

Apply to Group Secretary, 19, Alexandra-road, Barnstaple.

BARNSTAPLE. NORTH DEVON INFIRMARY. (105 Beds.) HOUSE PHYSICIAN (pre-registration) required in March.

Applications, naming 2 referees, to Group Secretary, 19, Alexandra-road, Barnstaple, N. Devon.

BARROW-IN-FURNESS. NORTH LONSDALE HOS-PITAL. Applications are invited for the resident post of HOUSE OFFICER (surgical) (recognised for pre-registration) at the North Lonsdale Hospital, Barrow-in-Furness. Post available immediately. Recognised for F.R.C.S.

Applications to the Group Secretary, Barrow and Furness Hospital Management Committee, 105, Abbey-road, Barrow-in-Furness.

BEBINGTON, CHESHIRE. CLATTERBRIDGE HOS-PITAL. CENTRAL WIRRAL GROUP.

HOUSE OFFICER (pædiatrics) for unit of 82 Beds. Recognised pre-registration and D.C.H.

HOUSE OFFICER (general medical and geriatrics). Recognised pre-registration.

HOUSE OFFICER (general surgery). Recognised pre-registration.

All posts are tenable 6 months from 1st March, 1958. Salary according to previous posts held.

Application forms, from Secretary, to be returned by 25th January, 1958.

BEBINGTON, CHESHIRE. CLATTERBRIDGE MATER-NITY HOSPITAL. (54 Beds.) CENTRAL WIRRAL GROUP. SENIOR HOUSE OFFICER (obstetrics and gynæcology). Salary according to previous posts held.

Application forms, obtainable from the Secretary, to be returned as soon as possible.

BECKENHAM HOSPITAL, Kent. Casualty Officer (Senior House Officer) required immediately for 1 year in first instance, with duties in Orthopædic and Fracture Departments. Recognised for F.R.C.S.

Apply, stating age, nationality, qualifications, and experience, and naming 3 referees, to Administrative Officer.

BEDFORD GENERAL HOSPITAL. (436 Beds.) House SURGEON post vacant immediately. Pre- or post-registration, recognised for F.R.C.S. Post offers exceptional opportunities for general experience in busy acute surgical units.

Applications, with copies of testimonials, to be sent immediately to Group Secretary, Bedford Group Hospital Management Committee, 3, Kimbolton-road, Bedford.

BIRMINGHAM (SANATORIA) GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER at West Heath Hospital, Rednal-road, Birmingham, 31, vacant 1st January, 1958. (207 Beds for the treatment of tuberculous and non-tuberculous chest cases.) The successful applicant will reside at the above Hospital (accommodation for single person only), and will be offered facilities for undertaking duties at the Birmingham Chest Clinic, Great Charles-street, Birmingham, 3.

Applications, stating age, qualifications, training and experience, together with copies of 3 recent testimonials, should be addressed to the Group Secretary, Birmingham (Sanatoria) Group Hospital Management Committee, Yardley Green Hospital, Birmingham, 9.

BIRMINGHAM AND MIDLAND EAR AND THROAT HOSPITAL, Edmund-street, BIRMINGHAM, 3. HOUSE OFFICER, resident (including pre-registration), required. Vacant 1st February, 1958.

Applications, with copies of recent testimonials, to Group Secretary, Dudley Road Hospital, Birmingham, 18.

BIRMINGHAM, 18. DUDLEY ROAD HOSPITAL. (775 Beds.) 2 HOUSE SURGEONS (general surgery). Recognised for pre-registration and F.R.C.S. Vacant now. Each appointment is in a unit of approximately 85 adult and children's general surgical beds under control of 2 Consultant Surgeons.

Applications marked House Surgeon to the Group Secretary, enclosing copies of 2 recent testimonials.

BIRMINGHAM. THE UNITED BIRMINGHAM HOS-PITALS. Applications are invited for the post of RESIDENT REGISTRAR in Anæsthetics to the United Birmingham Hospitals. The appointment is tenable for 1 year in the first instance. Preference will be given to candidates who have passed Part I, D.A., or Primary F.F.A. R.C.S.

Application forms may be obtained from the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15, and should be returned to him by 31st January, 1958.

BIRMINGHAM REGIONAL HOSPITAL BOARD AND UNITED BIRMINGHAM HOSPITALS. Whole-time SENIOR REGISTRAR in Radiodiagnosis. Duties at Coventry and Warwickshire Hospital and other hospitals in the Coventry group (9 notional half-days) and United Birmingham Hospitals (2 notional half-days). D.M.R.D. essential. Non-resident.

Application forms from Secretary, Regional Hospital Board, 10, Augustus-road, Birmingham, 15, to be returned by 3rd February, 1958.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

1. **Mid-Worcestershire Group. Birmingham-road, Bromsgrove**

REGISTRAR (casualty, required, also to deputise for Surgical Registrar, Kidderminster and District General Hospital (112 Beds). Experience specialty essential. Higher qualification desirable. Resident or non-resident.

2. **West Bromwich Group, Edward-street, West Bromwich**

(*a*) REGISTRAR (anæsthetics). Duties at West Bromwich and District General Hospital, Hallam Hospital, West Bromwich, and the Midland Centre for Neurosurgery, Smethwick. Experience specialty required. Married quarters available.

(*b*) Hallam Hospital, West Bromwich (456 Beds). Locum Tenens SURGICAL REGISTRAR. Resident. Salary £19 5s. p.w. less any charges. Commencing 6th February for approximately 3 months. Experience specialty essential.

Application forms from Group Secretaries to be returned, for 1 and 2 (*a*) by 27th January, 1958, and 2 (*b*) immediately.

BIRMINGHAM, 15. ROYAL ORTHOPÆDIC HOSPITAL. SENIOR HOUSE OFFICER. Preferably with orthopædic experience. Recognised by Royal College of Surgeons. 334 Beds for long- and short-term orthopædic cases (non-traumatic) and extensive outpatient services.

Applications, with testimonials or names of referees, to the Administrator.

BISHOP AUCKLAND. THE GENERAL HOSPITAL. SENIOR HOUSE OFFICER or JUNIOR HOSPITAL MEDICAL OFFICER ANÆSTHETIST required at the above Hospital. Grading according to qualifications and/or experience.

Applications, including names of 3 referees, to Group Secretary, South West Durham Hospital Management Committee, immediately.

BISHOP AUCKLAND. THE GENERAL HOSPITAL. HOUSE OFFICER (obstetrics and gynæcology). Applications invited from registered or pre-registration practitioners. Vacant 1st March, 1958. Recognised for D.Obst. R.C.O.G. Departmental beds 69.

Apply, naming 2 referees, to Group Secretary, South West Durham Hospital Management Committee, at above address.

BISHOP'S STORTFORD, HERTFORDSHIRE. HERTS AND ESSEX GENERAL HOSPITAL. (386 Beds.) SENIOR HOUSE OFFICER (surgical) required for general and orthopædic surgical duties. Salary £819 10s. p.a. less £150 in respect of resident emoluments. Appointment to commence 1st February, 1958.

Further particulars from, or applications with names of 2 referees to, the Hospital Secretary (Telephone: Bishop's Stortford 963).

BLACKBURN. ROYAL INFIRMARY. (262 general beds.) BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER or SENIOR HOUSE OFFICER (casualty and orthopædics) required immediately. Junior Hospital Medical Officer post can be for any period up to 4 years. Recognised for F.R.C.S.

Apply to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE.

Royal Infirmary, Blackburn

HOUSE SURGEONS (2) required for 25th January and 1st February, 1958. Posts recognised for F.R.C.S. and approved for pre-registration purposes.

Queen's Park Hospital, Blackburn

HOUSE SURGEON required for 1st February, 1958. Post recognised for F.R.C.S. and approved for pre-registration purposes.

Apply to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, WESTBOURNE. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the immediate appointment of SENIOR HOUSE OFFICER (resident), for E.N.T. duties. The appointment is recognised for the D.L.O. diploma and facilities are provided for studying.

Applications to the Hospital Secretary, Royal Victoria Hospital, Shelley-road, Bournemouth.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Shelley-road. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of GENERAL HOUSE SURGEON. The post which becomes vacant on 30th January, 1958, is recognised for the F.R.C.S. examination and for pre-registration purposes.

Application to the Hospital Secretary.

BRISTOL. MANOR PARK HOSPITAL. (650 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER. Salary £852 10s.–£55–£1182 10s. Furnished accommodation available, together with board and laundry, for which a charge of £170 p.a. is made. The Hospital caters for acute medical and chronic sick patients. Consultant staff visit regularly and there is ample time for post-graduate study.

Applications, stating age, nationality, whether married or single, experience, qualifications, and names and addresses of 2 referees, to be sent to the Group Secretary, Manor Park Hospital, Manor-road, Fishponds, Bristol, within 14 days of the appearance of this advertisement.

BRISTOL. SOUTHMEAD GENERAL HOSPITAL GROUP MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (pædiatrics) (resident) at Southmead Hospital for 12 months commencing 1st March, 1958. The post offers wide experience of general and neonatal pædiatrics and is associated with the University Departments of Child Health and Obstetrics. Preference will be given to candidates wishing to enlarge their experience in the care of the newborn.

Applications to be forwarded to the Group Secretary, Southmead Hospital, Bristol, not later than 31st January, 1958.

BRISTOL. COSSHAM/FRENCHAY HOSPITAL MANAGEMENT COMMITTEE. Frenchay Hospital. SENIOR HOUSE OFFICER, Regional Department of Neurosurgery. Vacancy occurs end of February, 1958, for the above post, tenable for 6 to 12 months. The post offers useful surgical experience and the opportunity of gaining a working knowledge of neurological diagnosis. Recognised for F.R.C.S.

Applications to the Secretary, Frenchay Hospital, quoting "N.S.F." 2 referees required.

BRIGHTON GENERAL HOSPITAL. Applications are invited for the appointment of HOUSE SURGEON to the Orthopædic Unit. Vacant 12th February, 1958. This post is recognised as a pre-registration appointment.

Applications, stating age, qualifications, and experience, and giving the names of 2 referees, should be sent to the Physician-Superintendent, Brighton General Hospital, Elm-grove, Brighton.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (314 Beds.) CASUALTY HOUSE SURGEON required 22nd January. Duties include work in Orthopædic and Traumatic Unit. Recognised for pre-registration and F.R.C.S.

Applications, stating usual particulars and naming two referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (314 Beds.) HOUSE SURGEON (including gynæcology) required 1st February, 1958. Pre-registration and recognised for F.R.C.S.

Applications, stating usual particulars, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRIGHTON. SUSSEX EYE HOSPITAL. (56 Beds.) HOUSE SURGEON required 11th February, 1958. Recognised for F.R.C.S. and D.O. Successful candidate will be considered for senior post (Senior House Officer) on completion of 6 months.

Applications, stating age, qualifications and experience and naming 2 referees, to the Administrative Officer.

BURLEY-IN-WHARFEDALE, ILKLEY. SCALEBOR PARK. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER (Male or Female) at Scalebor Park, a modern hospital of 450 Beds (Health Service, amenity and private), for the active treatment of nervous and mental disorders. The Hospital is associated for teaching purposes with the Department of Psychiatry of Leeds University, and facilities will be granted for attending the D.P.M. course. The salary is in accordance with the Whitley Council scale. A semi-detached house will be available for a married man, for which an agreed rental will be payable.

Applications to the Physician-Superintendent immediately.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEONS (3). Applications are invited for 3 pre-registration posts in General Surgery which will be falling vacant during January and February, 1958. 2 of the posts are at Bury General Hospital and the third at Rossendale General Hospital.

Apply, stating age, qualifications and other details, to the Group Secretary at Bury General Hospital, Bury, Lancs.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) The post of GENERAL SURGICAL AND UROLOGICAL HOUSE SURGEON (pre-registration or third post), which is recognised for the F.R.C.S., becomes vacant at the end of January, 1958. National Health Service salary and conditions.

Applications, together with copies of 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CANTERBURY. KENT AND CANTERBURY HOSPITAL. (277 Beds.) The post of OBSTETRIC HOUSE SURGEON, which is recognised for the M.R.C.O.G. and D.Obst.R.C.O.G., becomes vacant early in February, 1958. National Health Service salary and conditions.

Applications, together with 2 recent testimonials, to be addressed to the Hospital Secretary at the above Hospital.

CARLUKE, LANARKSHIRE. LAW HOSPITAL. Applications are invited for the posts of JUNIOR HOSPITAL MEDICAL OFFICER and HOUSE SURGEON in Orthopædic Surgery at Law Hospital, Carluke (790 Beds). The unit consists of 120 Beds and deals with acute orthopædic and accident work from a large part of Lanarkshire, and offers excellent experience.

Applications, giving full details, should be submitted to the Group Medical Superintendent, Law Hospital, Carluke.

CARLUKE, LANARKSHIRE. LAW HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER (medical) for 1st February, 1958.

Applications, stating age, qualifications and previous experience, together with the names of 2 referees, should be submitted to the Group Medical Superintendent, Law Hospital, Carluke.

CARLUKE, LANARKSHIRE. LAW HOSPITAL. Applications are invited for the post of RESIDENT HOUSE SURGEON (pre- or post-registration) for the 6 months commencing 1st February, 1958.

Applications, stating age, qualifications and any previous experience, together with the names of 2 referees, should be sent to the Group Medical Superintendent, Law Hospital, Carluke.

CATERHAM, SURREY. ST. LAWRENCE'S HOSPITAL. ST. LAWRENCE'S HOSPITAL GROUP MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR PSYCHIATRIC REGISTRAR required at above Hospital. The Hospital, approximately 20 miles from London, accommodation 2250 mentally defective patients of all ages and types, affords good facilities for study, and experience in pædiatrics, and has a research laboratory. Residential accommodation (single) available at the prescribed charge. Candidates may visit the Hospital by arrangement with the Physician-Superintendent.

Application forms obtainable from the Group Secretary. Completed forms (5 copies) to be returned to him by 31st January, 1958.

CAMBRIDGE. PAPWORTH HOSPITAL. Papworth HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER in the modern Thoracic Surgical Unit at above Hospital. The Unit, which contains the most up-to-date surgical and X-ray equipment, provides experience in a wide range of cardiac and pulmonary surgery.

Applications, giving details of previous experience, age, &c., together with names of referees, should be addressed to the Secretary, Papworth Hospital Management Committee, Papworth Hall, Cambridge.

CAMBRIDGE. THE UNITED CAMBRIDGE HOSPITALS. RESIDENT REGISTRAR (Male) at Brookfields Hostal, Cambridge. This Hospital has 2 wards for infectious diseases, 1 for general medicine and 1 for tuberculosis, and is the poliomyelitis centre for the south-west section of East Anglia. Appointment for 1 year in first instance, renewable for a second year.

Apply, with full particulars and names of 3 referees. to Secretary, Addenbrooke's Hospital, Cambridge, by 8th February.

CARSHALTON, SURREY. QUEEN MARY'S HOSPITAL FOR CHILDREN. (A general children's hospital of 550 Beds.) HOUSE SURGEON (Senior House Officer) required. (General surgery, E.N.T. and orthopædics.) Recognised for D.C.H.

Applications, stating age and qualifications, together with 1 recent testimonial and the names of 2 referees, should be submitted to the Group Secretary immediately.

CHELMSFORD AND ESSEX HOSPITAL. (161 Beds.) Applications are invited for the post of RESIDENT HOUSE SURGEON. Pre-registration post. The post offers good surgical experience. Recognised for the F.R.C.S.

Applications, together with 2 recent testimonials, to the Secretary, Chelmsford Hospital Management Committee, London-road, Chelmsford.

CHELMSFORD HOSPITAL MANAGEMENT COMMITTEE. Resident Locum MEDICAL REGISTRAR required for period 9th–22nd February.

Applications to Secretary, Chelmsford Hospital Management Committee, Chelmsford and Essex Hospital, London-road, Chelmsford, Essex.

CHELTENHAM GENERAL HOSPITAL. (220 Beds.) HOUSE SURGEON required (pre- or post-registration). Vacant now. The post offers a wide experience in general surgery, gynæcology, and orthopædic surgery. Post recognised for the F.R.C.S.

Applications, with names of 2 referees, to be sent to Secretary, General Hospital, Cheltenham.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL (late Botleys Park War Hospital). (430 Beds.) RESIDENT HOUSE SURGEON (Senior House Officer or Intern) required for Gynæcological (30 Beds) and E.N.T. (approximately 14 Beds) Departments. Salary in accordance with terms and conditions of National Health Service. Post vacant 1st February, 1958.

Applications, together with names and addresses of referees, to Physician-Superintendent, St. Peter's Hospital, as soon as possible.

CHICHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for appointment of SURGICAL REGISTRAR (Resident Surgical Officer) for 1 year (renewable) from 7th April for duty primarily at Royal West Sussex Hospital, Chichester (202 Beds.) Post recognised for F.R.C.S. 7 residents (4 surgical) of whom Resident Surgical Officer the senior. Salary £935 first year, £1061 10s. second, each less £170 for residence. Candidates may visit hospital.

Forms from Group Secretary, 174, Broyle-road, Chichester, to be submitted by 8th February.

COLCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for :—

Essex County Hospital, Colchester (189 Beds)

Post of HOUSE SURGEON. Recognised for F.R.C.S. First, second, third or pre-registration post, tenable for 6 months.

Post of Locum MEDICAL REGISTRAR for period 1st–28th February, 1958.

Black Notley Hospital, Braintree, Essex (516 Beds)

Post of HOUSE SURGEON. Includes duties in general surgical and gynæcological wards. Recognised for F.R.C.S. First, second, third or pre-registration post, tenable for 6 months.

Applications, with copies of 3 testimonials, to Group Secretary, Colchester Group Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

CREWE AND DISTRICT MEMORIAL HOSPITAL. (108 Beds acute, and continuation 32 Beds.) Pre-registration HOUSE OFFICER (surgical) required. Approved for F.R.C.S. Married quarters available. Vacant early February. On completion, this post could be followed by pre-registration obstetrics post (approved for D.Obst.R.C.O.G.).

Applications, stating age, qualifications, &c., with names of 2 referees, to be sent to the Group Secretary, South Cheshire Hospital Management Committee, Barony Hospital, Nantwich, Cheshire, within 7 days after publication.

DARLINGTON (near). AYCLIFFE HOSPITAL FOR MENTAL DEFECTIVES, AYCLIFFE HOSPITAL, HEIGHINGTON, near DARLINGTON, CO. DURHAM. Locum JUNIOR HOSPITAL MEDICAL OFFICER required for an approximate period of 6 weeks commencing on 10th March, 1958, at the above Hospital. Salary £19 5s. per week, less an amount of £3 5s. 2d. per week in respect of residential accommodation.

Applications to the Medical Superintendent.

T. H. ALLAN, Group Secretary.

CUCKFIELD HOSPITAL, Cuckfield, near Haywards HEATH, SUSSEX. RESIDENT SENIOR HOUSE OFFICER (general surgery). Post vacant 11th February. Tenable 6 months in first instance.

Applications, stating age, qualifications, nationality and experience, with names of 2 referees, to Group Secretary, Mid-Sussex Hospital Management Committee.

CUCKFIELD HOSPITAL, Cuckfield, near Haywards HEATH, SUSSEX. HOUSE SURGEON (orthopædic and traumatic unit). Post vacant 22nd January.

Applications, giving age, nationality, qualifications and experience, and names of 2 referees, to Group Secretary, Mid-Sussex Management Committee.

DERBY. CITY HOSPITAL. (260 Beds. Recognised for training in obstetrics for D.Obst.R.C.O.G. and M.R.C.O.G.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (obstetrics) required. Appointment for 1 year in the first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 27th January, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

DERBY. CITY HOSPITAL. Derby No. 1 Hospital MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER in Surgery. This post is recognised for the F.R.C.S. Vacant beginning of March.

Applications, stating full details, together with copies of 2 recent testimonials, should be sent to the Medical Superintendent, City Hospital, Derby, as soon as possible.

DERBY. CITY HOSPITAL. Derby No. 1 Hospital Manage-MENT COMMITTEE. Applications are invited for the posts of HOUSE SURGEONS (2 vacancies) (pre-registration) or SENIOR HOUSE OFFICER (surgical). Posts vacant early in March.

Applications, stating full details, together with copies of 2 recent testimonials, should be sent to the Medical Superintendent, City Hospital, Derby, as soon as possible.

DERBY. CITY HOSPITAL. Derby No. 1 Hospital Manage-MENT COMMITTEE. Applications are invited for the post of HOUSE PHYSICIAN (Senior House Officer) (medicine) for duties in General Medicine and Pædiatrics. Post vacant early in March.

Applications, stating full details, together with copies of 2 recent testimonials, should be sent to the Medical Superintendent, City Hospital, Derby, as soon as possible.

DERBY. CITY HOSPITAL. Derby No. 1 Hospital Manage-MENT COMMITTEE. Applications are invited for the post of HOUSE PHYSICIAN (pre-registration) or SENIOR HOUSE OFFICER (medicine) for duties in General Medicine. Post vacant early in March.

Applications, stating full details, together with copies of 2 recent testimonials, should be sent to the Medical Superintendent, City Hospital, Derby, as soon as possible.

DERBY. DERBYSHIRE HOSPITAL FOR WOMEN. (72 Beds. Recognised for training for M.R.C.O.G.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (gynæcology) required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 27th January, 1958, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

DERBY. DERBYSHIRE ROYAL INFIRMARY. (417 Beds.) SENIOR HOUSE OFFICER (orthopædic). Vacant immediately. Recognised for 6 months' "unspecified" training for F.R.C.S.

Apply, giving full details and 2 names for reference, to Secretary.

DONCASTER ROYAL INFIRMARY. (330 Beds.) Applications are invited for the post of HOUSE SURGEON (Intern or Senior House Officer). Post recognised for F.R.C.S.

Applications, stating age, &c., and enclosing copies of 2 recent testimonials, to the Group Secretary, Doncaster Hospital Management Committee, at Doncaster Royal Infirmary.

DORCHESTER. DORSET COUNTY HOSPITAL. (109 Beds.) HOUSE SURGEON required for resident, pre-registration post vacant mid-January and tenable for 6 months. Recognised for F.R.C.S. examinations.

Applications, stating age and qualifications, together with copy testimonials, to Group Secretary, West Dorset Hospital Management Committee, Damers-road, Dorchester, Dorset, immediately.

DUDLEY, STOURBRIDGE AND DISTRICT HOSPITAL GROUP, BIRMINGHAM REGION.

The Guest Hospital, Dudley (154 Beds)

HOUSE OFFICER (medical), pre-registration. Post vacant now.

The Corbett Hospital, Stourbridge (114 Beds)

HOUSE OFFICER (surgical), pre-registration. Post vacant January, 1958.

Wordsley Hospital, near Stourbridge (478 Beds)

HOUSE OFFICER (surgical), pre-registration. Post vacant January, 1958.

Prestwood Sanatorium, near Stourbridge (199 Beds. Tuberculosis)

Locum JUNIOR HOSPITAL MEDICAL OFFICER, resident, required for a period of 1 year.

Apply Group Secretary, Guest Hospital, Dudley, Worcs.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. REGISTRAR in Chest Medicine, Ipswich Chest Clinic and St. Helen's Hospital, Ipswich (resident—house available). Preference will be given to candidates with an interest in the epidemiology of tuberculosis. Duties will include work with the new Community X-ray Survey Unit and the Associated School Tuberculosis Survey. Clinical duties in chest medicine and in infectious disease will include work in the Outpatient Department and the wards of St. Helen's Hospital. Appointment for 1 year, renewable for second year.

Applications, stating age, experience and the names of 3 referees, to the Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 3rd February, 1958. Candidates invited to visit the hospital by direct arrangement with Hospital Management Committee. Secretary, Ipswich and East Suffolk Hospital, Anglesea-road Wing, Ipswich.

EAST GRINSTEAD. QUEEN VICTORIA HOSPITAL. RESIDENT HOUSE OFFICER (Male or Female) required immediately for General Hospital. Appointment for 6 months in first instance. Recognised for pre-registration purposes, and for F.R.C.S. examination.

Apply, stating age and experience, with names of 3 referees, to Hospital Secretary.

EPPING. ST. MARGARET'S HOSPITAL. Resident SENIOR HOUSE OFFICER (surgery). Post vacant early February. Recognised for F.R.C.S. Busy general hospital with easy access to London.

Applications, with copies of 2 testimonials, to reach the Group Secretary, Epping Group Hospital Management Committee, "Oak Cottage", The Plain, Epping, Essex, by 22nd January, 1958.

EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom, SURREY. RESIDENT HOUSE SURGEON required 12th February. Pre-registration post, recognised for F.R.C.S.

Applications, stating age, qualifications, and experience, with copies of 2 recent testimonials, should be sent as soon as possible to Group Secretary at above address.

EPSOM. THE MENTAL HOSPITALS GROUP LABORATORY. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for non-resident, Whole-time REGISTRAR in Pathology. The Laboratory affords excellent facilities for training and experience in all branches of pathology with opportunities for specialisation and research. In addition to working at the Laboratory, the person appointed will be required to visit and work at the hospitals served by the Laboratory.

Application forms may be obtained from the Group Pathologist, Mental Hospitals Group Laboratory, at West Park Hospital, Epsom, from whom full information may be obtained and with whom an appointment to see the laboratory may be arranged. Closing date for applications 1st February, 1958.

GLASGOW, E.1. EASTERN DISTRICT HOSPITAL. HOUSE OFFICERS (2) required for Surgical Unit of Eastern District Hospital for the period February to July, 1958. Pre-registration posts. Active unit and busy Outpatient Department.

Applications to Medical Superintendent.

GRAVESEND AND NORTH KENT HOSPITAL, Gravesend. MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON. Applications are invited for this resident post, vacant now; approved under pre-registration regulations and tenable for 6 months. Post offers experience also in obstetrics, gynæcology, and orthopædics. Salary £467 10s.–£577 10s. p.a., according to experience.

Applications to Hospital Secretary, giving details of experience, age, qualifications, and nationality.

GRAVESEND AND NORTH KENT HOSPITAL, Gravesend, KENT. MEDWAY AND GRAVESEND HOSPITAL MANAGEMENT COMMITTEE. Locum HOUSE SURGEON required immediately. Salary £10 9s. per week.

Applications to Hospital Secretary.

HARROGATE AND DISTRICT GENERAL HOSPITAL, HARROGATE, YORKSHIRE. (253 Beds.) HOUSE PHYSICIAN, vacant 1st February, 1958. Approved pre-registration post. Pleasantly situated modern hospital.

Applications immediately, with names of 2 referees, to Hospital Secretary.

HEMEL HEMPSTEAD, HERTFORDSHIRE. WEST HERTS HOSPITAL. 2 HOUSE SURGEONS (pre-registration) required.

Applications, giving full details and 2 names for reference, should be sent to the Hospital Secretary as soon as possible.

HERTFORD COUNTY HOSPITAL. (171 Beds. Hospital situated 21 miles from London.) Applications are invited for the appointment of HOUSE SURGEON (general, gynæcology and obstetrics). First or second post. To commence as soon as possible. Pre-registration post; recognised under F.R.C.S. regulations.

Applications to Group Secretary, Hertford Hospital Management Committee, County Hospital, Hertford, Herts.

HERTFORD COUNTY HOSPITAL. (171 Beds. Hospital situated 21 miles from London.) Applications are invited for appointment of RESIDENT HOUSE PHYSICIAN (Male or Female), second post held. Recognised pre-registration post. 6 months' appointment. Preference given to applicants who have held resident surgical or medical posts in general hospital. Duties to commence mid-February, 1958.

Applications to Group Secretary, Hertford Hospital Management Committee, County Hospital, Hertford, Herts.

HEXHAM GENERAL HOSPITAL, Northumberland. (304 Beds.) HOUSE SURGEONS (pre- or post-registration) or SENIOR HOUSE OFFICERS (surgery) according to experience, required immediately. Posts are combined with orthopædics, providing excellent experience. Recognised for F.R.C.S.

Applications, with names of 2 referees, to Group Secretary, General Hospital, Hexham, Northumberland.

HASTINGS AND ST. LEONARDS-ON-SEA. BUCHANAN HOSPITAL. (91 Beds.) HOUSE SURGEON required for gynæcological beds (32) in hospital for obstetric and gynæcological patients only. Appointment recognised for M.R.C.O.G. is vacant Monday, 24th February, 1958. Candidates for pre-registration service (surgery) can be considered.

Applications, giving names and addresses of 3 referees, to be sent to the Hospital Administrator.

HASTINGS HOSPITAL MANAGEMENT COMMITTEE. Locum ORTHOPÆDIC REGISTRAR required for whole-time duties from 11th January, 1958. Remuneration £19 5s. per week. Non-resident.

Apply, giving details of qualifications and experience, to Group Secretary, 11, Holmesdale-gardens, Hastings, as soon as possible.

HASTINGS. ST. HELEN'S HOSPITAL. (493 Beds.) SENIOR HOUSE OFFICER in Geriatrics required. Resident.

Apply to Hospital Administrator.

HASTINGS. ST. HELEN'S HOSPITAL. (493 Beds.) HOUSE SURGEON required. Pre-registration post recognised for F.R.C.S. Modern theatre.

Applications to Hospital Administrator.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required to commence duty immediately. The post is recognised as a pre-registration appointment and for the F.R.C.S. Salary in accordance with national scale.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON,
Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from provisionally registered medical practitioners for the post of HOUSE PHYSICIAN, to commence duties on 1st March, 1958. Salary in accordance with national scales.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON,
Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

HUDDERSFIELD. ST. LUKE'S HOSPITAL. (235 Beds.) Applications are invited for the post of RESIDENT MEDICAL OFFICER (Junior Hospital Medical Officer grade) at the above Hospital, to commence duties immediately. The Group Geriatric Admission Unit is based on this Hospital, which also caters for acute medical and surgical, pædiatric and maternity patients. Salary in accordance with the terms and conditions of service for hospital medical and dental staff, £852 10s.–£55–£1182 10s. p.a. House available for married candidate.

Applications, together with copies of 3 recent testimonials, to be sent to the undersigned as soon as possible.

H. J. JOHNSON,
Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

ILFORD. KING GEORGE HOSPITAL, Eastern-avenue. There will be a vacancy for a HOUSE PHYSICIAN at above Hospital on 21st February, 1958. 1st or 2nd post pre-registration. The post will be tenable for 6 months.

Applications, giving full particulars and accompanied by testimonials, should be sent to the undersigned within 7 days of the appearance of this advertisement.

H. F. HARRIS, Group Secretary Ilford, and
Barking Group Hospital Management Committee.

King George Hospital.

IPSWICH AND EAST SUFFOLK HOSPITAL (Anglesea-ROAD WING). (356 Beds.) Applications are invited for 2 posts of HOUSE SURGEON to Consultant General Surgeons, both vacant mid-January. The posts are recognised for pre-registration and for the F.R.C.S. examinations.

Applications, with copies of recent testimonials, to Hospital Secretary.

KETTERING AND DISTRICT GENERAL HOSPITAL. CASUALTY OFFICER (Senior House Officer). Recognised for F.R.C.S. The post, vacant now, offers wide experience of all traumatic conditions including fractures and some orthopædic cases with charge of 30 Beds.

Applications, accompanied by testimonials, to be sent to the Group Secretary, General Hospital, Kettering.

LEICESTER. TOWERS MENTAL HOSPITAL. (1168 Beds.) Applications are invited for the whole-time post of JUNIOR HOSPITAL MEDICAL OFFICER. Salary £852 10s.–£55–£1182 10s. There is ample opportunity for experience in all branches of psychiatry including outpatient work and the Hospital is recognised for D.P.M. experience. Facilities for post-graduate training exist at Sheffield University. Resident accommodation is available for a single man or woman, for which the appropriate charge will be made. Candidates must have completed their service with H.M. Forces.

Applications, giving age, nationality, and full details with the names of 2 referees, to be sent to the Medical Superintendent as soon as possible.

LEEDS REGIONAL HOSPITAL BOARD. Registrar vacancies

Anæsthetics

Hull A, B, and East Riding Groups. Recognised for the F.F.A. R.C.S. Duties may include thoracic anæsthesia. Non-resident. Post vacant 1st April, 1958.

General Medicine

St. James's Hospital, Leeds (206 general medical beds). Duties those of Resident Medical Officer. Post vacant 1st April, 1958.

General Surgery

Dewsbury, Batley and Mirfield Group (120 general surgical beds), may include some duties in the Casualty Department. Resident.

Hull Royal Infirmary (80 general surgical beds), and other hospitals in the Hull A Group. Duties those of Resident Surgical Officer and includes additional duties in the Casualty Department.

Otley General Hospital (42 general surgical beds). Recognised for the F.R.C.S. Consultant staff mainly from Leeds Teaching Hospital. (Resident married quarters available.) Post vacant 1st April, 1958.

Applications, stating age, qualifications and details of present and previous appointments with dates, together with the names and addresses of 3 referees, to the Secretary, the Joint Registrars Committee, Park-parade, Harrogate, by 29th January, 1958.

LEEDS. THE UNITED LEEDS HOSPITALS. THE GENERAL INFIRMARY AT LEEDS. RESIDENT ORTHOPÆDIC OFFICER required, of Senior House Officer status. The post will be initially for 6 months and will be renewable for a further period of 6 months thereafter. Terms and conditions of service for hospital medical staff apply.

Applications, stating age, qualifications, previous posts with dates, and 3 names for reference, to be sent to the Secretary to the Board by not later than 23rd January, 1958.

LEEDS. THE UNITED LEEDS HOSPITALS. THE GENERAL INFIRMARY AT LEEDS. SENIOR HOUSE OFFICER in E.N.T. Department required for a period of 6 months. Terms and conditions of service for hospital medical staffs apply.

Applications, giving details of age, qualifications, posts held, with dates, and 3 names for reference, should be sent to the Secretary to the Board, The General Infirmary, Leeds, 1, by not later than 23rd January, 1958.

LINCOLN COUNTY HOSPITAL, Sewell-road. (200 Beds.) Applications are invited from pre-registration candidates for appointment as HOUSE SURGEON for 6 months, commencing in February, 1958, to be followed, if satisfactory, by appointment as House Physician for a further 6 months.

Full particulars should be sent to R. W. HOWICK, Group Secretary.

LIVERPOOL, 6. NEWSHAM GENERAL HOSPITAL. Applications are invited for the appointment of HOUSE PHYSICIAN (pre-registration) or SENIOR HOUSE OFFICER. Grading according to experience. The appointment is tenable from 1st March, 1958, approximately and may be resident or non-resident.

Applications and inquiries to the Physician-Superintendent at the Hospital. H. BLYTHE, Group Secretary.

LOWESTOFT AND NORTH SUFFOLK HOSPITAL, LOWESTOFT, SUFFOLK. SENIOR HOUSE SURGEON (resident) required immediately. Furnished flat available for married officer, if desired. Post recognised for Final F.R.C.S. examination requirements. The Hospital has a Consultant General Surgeon and is regularly visited by Consultants in all specialties from the Norfolk and Norwich Hospital. Membership of a Medical Defence Society is a condition of appointment.

Applications, stating age, qualifications and experience, with names and addresses of 2 referees, to Hospital Secretary.

LUTON AND DUNSTABLE HOSPITAL, Luton, Bedfordshire. HOUSE SURGEON, post now vacant. Tenable for 6 months. Recognised as pre-registration post and for F.R.C.S.

Applications stating age, nationality, qualifications and experience, together with copies of two recent testimonials, to the Secretary of the Hospital.

LYMINGTON HOSPITAL, Lymington, Hampshire. (95 Beds.) RESIDENT SENIOR HOUSE OFFICER (medical) required 1st February, 1958.

Applications, with copies of testimonials, should be forwarded as soon as possible to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

MACCLESFIELD HOSPITAL (West Park Branch). (204 Beds.) Applications invited resident pre-registration post OBSTETRICS/GYNÆCOLOGY HOUSE OFFICER, vacant 1st February, 1958. Recognised D.Obst.R.C.O.G., training. 23 obstetric, 30 gynæcological beds. Also resident pre-registration post GENERAL MEDICINE. Vacant 1st February, 1958. Department has 62 acute beds. Excellent opportunities for gaining valuable experience.

Apply immediately for both posts, with full particulars and names of 2 referees, to Group Secretary, Macclesfield and District Hospital Management Committee, "Willerby House", Cumberland-street, Macclesfield.

MAIDENHEAD HOSPITAL, St. Luke's-road, Maidenhead. RESIDENT SURGICAL REGISTRAR. The appointment is recognised for the final examination for the Fellowship of the Royal College of Surgeons, and the successful candidate will gain excellent experience in general surgery. There are 4 other Residents, including a House Surgeon and a Casualty Officer.

Application forms may be obtained from the Secretary, Windsor Group Hospital Management Committee, Alma-road, Windsor, and should be completed and returned by 25th January.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (141 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the pre-registration post of HOUSE SURGEON. 6 months' appointment. Post vacant mid-January, 1958. Salary at the rate of £467 10s.–£577 10s. A deduction at the rate of £125 a year is made for board and lodging, and other services provided.

Applications should be forwarded, as soon as possible, to the Administrative Officer at the Hospital.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (141 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. CASUALTY OFFICER (Senior House Officer). Recognised for F.R.C.S. Salary £819 10s. p.a. less £150 p.a. for board and lodging. Post vacant February, 1958.

Applications to the Administrative Officer at the Hospital.

MAIDSTONE. KENT COUNTY OPHTHALMIC AND AURAL HOSPITAL. (113 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE SURGEON in the E.N.T. Department of the above Hospital. Post vacant end of January, 1958. There are 55 E.N.T. beds and 6 specialist operating sessions each week. Valuable experience is available, and the post is recognised for the purpose of the F.R.C.S. and the D.L.O. Salary will be £819 10s. a year, less £150 a year for residential emoluments.

Applications to the Administrative Officer, Kent County Ophthalmic and Aural Hospital, Maidstone, Kent.

MANCHESTER REGIONAL HOSPITAL BOARD. Blackburn Royal Infirmary. REGISTRAR (medicine) required 3rd February, 1958. Resident post. Duties at Royal Infirmary, Blackburn (262 acute beds) as arranged by Consultant Physician.

Application forms from Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn, Lancs.

MANCHESTER REGIONAL HOSPITAL BOARD. South Manchester Hospital Management Committee. Applications are invited from registered medical practitioners for the post of REGISTRAR in Radiotherapy at the Christie Hospital and Holt Radium Institute, Manchester. Candidates must hold either the Diploma in Radiotherapy or an F.R.C.S. or M.R.C.P.

Applications, with full details, to be forwarded to the Group Secretary, Withington Hospital, Manchester, immediately.

MANCHESTER REGIONAL HOSPITAL BOARD. Applications are invited for the full-time post of ORTHOPÆDIC REGISTRAR in the Ashton, Hyde and Glossop Group of Hospitals, with duties mainly at Ashton-under-Lyne General Hospital. There are approximately 40 orthopædic beds and busy orthopædic and casualty outpatients departments. The post is recognised for additional training under F.R.C.S. regulations.

Applications, stating age, nationality, qualifications and experience, with copies of 2 references, should be forwarded to the Group Secretary, Ashton, Hyde and Glossop Hospital Management Committee, General Hospital, Ashton-under-Lyne, Lancashire, as soon as possible.

MANCHESTER REGIONAL HOSPITAL BOARD. Blackburn and District Hospital Management Committee. RESIDENT REGISTRAR (obstetrics/gynæcology) required 1st February, 1958. Post recognised for Membership and D.Obst.R.C.O.G. (combined obstetrics and gynæcology). Based on Queen's Park Hospital, Blackburn, a large busy hospital with 58 obstetric and 29 gynæcology beds. Duties also at Royal Infirmary, Blackburn, and Victoria Hospital, Accrington. Accommodation may be available for a married man.

Application forms available from and returnable to the Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the post of REGISTRAR in Thoracic Surgery to the Blackpool and Fylde Group of hospitals with main duties at the Victoria Hospital, Blackpool. The post available from 1st February is recognised for the F.R.C.S. and offers a sound experience gained with the 2 Consultant Thoracic Surgeons who are responsible for the thoracic surgery in the northern part of the Manchester Region. Non-resident post but residential accommodation is available if required for single applicants.

Applications, stating age, qualifications and experience, together with the names and addresses of 2 referees, should be sent to the Group Secretary, Victoria Hospital, Blackpool.

MANCHESTER REGIONAL HOSPITAL BOARD. South Manchester Hospital Management Committee, Baguley Hospital. (402 Beds.) The Board invite applications for the post of REGISTRAR in Chest Diseases. This Hospital is a large thoracic unit fully equipped for the medical and surgical treatment of tuberculosis and other chest diseases. Attached to the Hospital is a Chest Clinic. The post offers opportunities for wide experience in medical and surgical treatment of patients suffering from tuberculosis and other diseases of the chest, together with chest clinic work. Ample scope for clinical research.

Applications, stating age, qualifications, nationality, experience and the names of 2 referees, to be forwarded to the Group Secretary, Withington Hospital, Manchester, 20, within 7 days of appearance of this advertisement.

MANCHESTER, 20. CHRISTIE HOSPITAL AND HOLT RADIUM INSTITUTE. South Manchester Hospital Management Committee. Applications are invited from resident medical practitioners for the post of RESIDENT SENIOR HOUSE OFFICER (radiotherapy) at the above Hospital. Suitable applicants will be eligible for the D.M.R.T. course commencing in April, 1958.

Applications, with full details and the names of 2 referees, to the Group Secretary, Withington Hospital, Manchester, 20, immediately.

MANCHESTER, 20. GROUP PATHOLOGY LABORATORY, WITHINGTON HOSPITAL. South Manchester Hospital Management Committee. Applications are invited for the post of RESIDENT PATHOLOGIST (Senior House Officer grade). Vacant now. Tenable for 12 months. Previous experience in pathology not essential, the post affording opportunities for gaining experience in all branches of clinical pathology. Laboratory recognised for the Dip. Path.

Applications, stating age, qualifications, present post, experience and the names of 2 referees, to be forwarded to the Group Secretary immediately.

MANCHESTER, 20. WITHINGTON HOSPITAL. South Manchester Hospital Management Committee. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER to the Regional Oral Surgery and Maxillo-Facial Unit at the above Hospital. The post provides every opportunity to study for F.D.S. and has R.C.S. recognition.

Applications, with full details, including the names of 2 referees, should be forwarded to the Group Secretary.

MANCHESTER. UNITED MANCHESTER HOSPITALS. Saint Mary's Hospitals, Manchester. Applications are invited for the post of RESIDENT CLINICAL PATHOLOGIST (Senior House Officer grade). Candidates must have held house appointments but previous laboratory experience is not essential. Suitable for candidates interested in obstetrics and/or paediatrics wishing to obtain laboratory experience. The duties will be mainly in the Department of Clinical Pathology, Saint Mary's Hospitals, but the holder of the post will also spend some time in the Manchester Royal Infirmary.

Application to be made on forms obtainable from the undersigned and submitted by 31st January, 1958.

A. R. WISE, General Superintendent.

Saint Mary's Hospitals, Whitworth Park, Manchester, 13.

MEXBOROUGH. MONTAGU HOSPITAL AND ANNEXE. (168 Beds and 30 Beds.) RESIDENT HOUSE SURGEON.

Applications to the Secretary, Hospital Management Committee, "Fern Bank", Doncaster-road, Rotherham.

MIDDLESBROUGH. NORTH ORMESBY HOSPITAL. Tees-side Hospital Management Committee. Applications are invited for the post of HOUSE OFFICER (surgery) for Surgical Team No. 2 (30 Beds) at the above Hospital. The post is recognised for pre-registration service under the Medical Act, 1950.

Applications, stating full details and giving 2 names for reference, should be addressed to the Hospital Secretary as soon as possible.

MIDDLESBROUGH. NORTH ORMESBY HOSPITAL. TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE PHYSICIAN, Male or Female, at the above Hospital. The medical unit consists of 52 beds and has an establishment for 2 pre-registration House Physicians, 1 post being already occupied.

Applications, stating age, qualifications, and experience, together with names of 2 referees, should be addressed to the Hospital Secretary.

MORECAMBE. QUEEN VICTORIA HOSPITAL. Senior HOUSE OFFICER (obstetrics and gynæcology). Post vacant now.

Applications, with names of 2 referees, to Group Secretary, Royal Lancaster Infirmary.

NEWCASTLE REGIONAL HOSPITAL BOARD. REGISTRAR ANÆSTHETIST, whole-time, Tees-side Group of hospitals—main hospital, North Ormesby (194 Beds). Non-resident, near main hospital. Post recognised for F.F.A.R.C.S. examination.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. Resident REGISTRAR in Anæsthetics for duties at hospitals in the Sunderland area (1947 Beds). Post offers practical experience under supervision of visiting anæsthetists, and is recognised for F.F.A.R.C.S. and D.A. Opportunity will be given to attend Newcastle Medical School for lectures.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. REGISTRAR PHYSICIAN, whole-time, 1 year only, Cardiovascular Unit, Newcastle General Hospital. Excellent experience afforded. Post available from 1st February, 1958. Single accommodation available.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. REGISTRAR ORTHOPÆDIC SURGEON, whole-time, Durham Group of hospitals—main hospital, County Hospital, Durham (116 Beds). Single accommodation available.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NORTHAMPTON. ST. ANDREW'S HOSPITAL. Applications are invited for the appointment of SENIOR REGISTRAR. Previous experience in psychiatry and possession of the D.P.M. are essential. The successful candidate will work in the Hospital and at outpatient clinics. Salary £1010 rising to £1340 p.a., together with full residential emolument, or if married unfurnished house, light, coal, laundry and garden produce, valued for superannuation purposes at £200 p.a. The Hospital operates outside the National Health Service but reciprocity has been granted between the National Health Service superannuation scheme and the Hospital superannuation scheme, so that years of service are transferable in either direction.

Applications, stating age, qualifications, experience, &c., together with copies of 3 recent testimonials, to be addressed to the Medical Superintendent.

NORTHAMPTON. ST. CRISPIN HOSPITAL, Duston, NORTHAMPTON. (1100 Beds.) SENIOR HOUSE OFFICER required. Salary according to national scale (£819 10s. p.a.). Accommodation is available at the hospital. The hospital is approved for training for the D.P.M. of the Conjoint Board and the post offers excellent opportunities for participation in inpatient and outpatient work, E.E.G. investigations and child psychiatry. There is a modern admission unit and an annual admission-rate of over 850 patients annually. Regular case conferences are held.

Applications, giving full details and names of 3 referees, to be sent to the Physician-Superintendent at the hospital within 14 days.

NORTHAMPTON GENERAL HOSPITAL. (500 Beds.) Vacancy 1st February, 1958, for SENIOR HOUSE OFFICER, E.N.T. Department. Recognised for F.R.C.S. and for D.L.O. Appointment to 30th September, 1958, in first instance.

Applications as soon as possible to S. G. HILL, Superintendent.

NOTTINGHAM CITY HOSPITAL. (811 Beds.) Applications are invited for the post of HOUSE SURGEON, vacant 15th February, 1958. Recognised for pre-registration purposes.

Applications, stating age, nationality, qualifications and experience, together with copies of not more than 3 testimonials, to be sent to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM CITY HOSPITAL. (811 Beds.) Applications are invited for the post of HOUSE PHYSICIAN vacant on 15th February, 1958. Recognised for pre-registration purposes.

Applications, stating age, nationality, qualifications and experience, together with copies of not more than 3 testimonials, to be sent immediately to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM CITY HOSPITAL. (811 Beds.) Applications are invited for the post of RESIDENT PATHOLOGIST (Senior House Officer). Previous experience an advantage. Post vacant immediately.

Applications, stating age, nationality, qualifications and experience, together with copies of not more than 3 testimonials, to be sent to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM. FIRS MATERNITY HOSPITAL. (40 Beds.) Required RESIDENT SENIOR HOUSE OFFICER (obstetrics). Post vacant 8th March, 1958. Recognised for D.Obst.R.C.O.G. Previous experience in obstetrics an advantage.

Applications, with copies of 3 testimonials, to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER (casualty), duties to commence about 3rd February. Establishment 3. Recognised for F.R.C.S. Post offers wide experience of casualty work.

Applications, stating age, nationality, qualifications and experience, together with copies of testimonials, to be sent to the Secretary, General Hospital, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. Resident Pre-registration HOUSE SURGEONS required, 4th February, 5th February.

Applications, stating age, qualifications and experience, together with copies of testimonials, to be sent to the Group Secretary.

NORWICH (near). LITTLE PLUMSTEAD MENTAL DEFICIENCY HOSPITAL. (1000 Beds.) Applications are invited for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER. The Hospital is modern, has a large outpatient service and admits many young patients for short periods for physical and mental investigation. Interest in physical medicine is encouraged. Married or single quarters available.

Applications, with the names and addresses of 2 referees, to the Medical Superintendent, Little Plumstead Hospital, near Norwich, Norfolk, by 31st January, 1958.

NORWICH. NORFOLK AND NORWICH HOSPITAL. Applications are invited for the following appointments, vacant 1st February, 1958. Both are pre-registration posts :—

(1) **Jenny Lind Hospital**

HOUSE SURGEON (Male or Female) at this Hospital, which forms the entire Pædiatric Department of the United Norwich Hospitals. The duties are under the direct supervision of the Consultant Staff of the Norfolk and Norwich Hospital. Post recognised for D.C.H. examination requirements.

(2) **West Norwich Hospital**

HOUSE SURGEON (Male or Female). Post recognised for final F.R.C.S. examination requirements. Duties general surgical and including burns and plastic work. The beds at this Hospital are under the control of the Consultant Staff of the Norfolk and Norwich Hospital.

Membership of a Medical Defence Society is a condition of appointment.

Applications, giving full details, with names of 2 referees, to Group Secretary, Hospital Management Committee, St. Stephen's-road, Norwich, immediately.

NORWICH. ST. ANDREW'S HOSPITAL MANAGE-MENT COMMITTEE. Applications are invited for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER (Male) for duty at the Mental Hospital of 240 Beds at Great Yarmouth which is to be attached to the St. Andrew's Group as from 1st April, 1958. Accommodation available for a single or married man. National Health Service salaries and conditions apply. Previous experience in psychiatry desirable but not essential.

Further particulars may be obtained from the Medical Superintendent, St. Andrew's Hospital, Thorpe, Norwich, to whom applications, giving details of age, qualifications, experience, and the names of 2 referees, should be addressed as soon as possible.

NUNEATON. GEORGE ELIOT HOSPITAL. House OFFICER in pædiatrics. Vacant now. Recognised pre-registration and D.C.H.

Applications to Hospital Secretary.

OXFORD REGIONAL HOSPITAL BOARD. Senior REGISTRAR in Psychiatry at St. Crispin Hospital, Duston, Northampton. Married accommodation available. Appointment for 1 year in the first instance, and, subject to satisfactory service, renewable for up to 4 years. It may be possible to arrange transfer to another mental hospital in the Oxford Region for the second half of the appointment. St. Crispin Hospital provides full training facilities, including Electroencephalography Department and participation in child guidance work. Applicants should hold the D.P.M.

Applications, on forms obtainable from the Secretary, Committee for Senior Registrars, 43, Banbury-road, Oxford, should reach him by 1st February.

OXFORD. UNITED OXFORD HOSPITALS. Applications invited for post of SENIOR HOUSE OFFICER in the Anæsthetic Department at the Radcliffe Infirmary, with effect from 27th January, 1958, for a period of 6 months.

Applications, stating age, qualifications and experience, together with names of 2 referees, to Administrator, Radcliffe Infirmary, Oxford, by 23rd January.

OXFORD. WARNEFORD AND PARK HOSPITALS. SENIOR HOUSE OFFICER required (resident). Warneford Hospital, 72 Beds ; Warneford Clinic (de-designated) 78 Beds ; and Park Hospital for Children, 30 Beds, with Outpatient Departments, give comprehensive psychiatric experience and training facilities. Accommodation for single person.

Apply before 25th January, 1958, to the Physician-Superintendent, with names of 2 referees.

PAISLEY AND DISTRICT MATERNITY UNIT. House OFFICERS required for above Unit, term commencing 1st February, 1958.

Applications to Group Medical Superintendent, Royal Alexandra Infirmary, Paisley.

PAISLEY. ROYAL ALEXANDRA INFIRMARY. House SURGEON required for Orthopædic Unit, term commencing 1st February, 1958.

Applications to Group Medical Superintendent.

PAISLEY. ROYAL ALEXANDRA INFIRMARY. House SURGEONS required for General Surgical Unit, term commencing 1st February, 1958.

Applications to Group Medical Superintendent.

PETERBOROUGH. THE MEMORIAL HOSPITAL. PETERBOROUGH AND STAMFORD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON (general surgery). Vacant 1st March, 1958.

Applications, with testimonials, should be addressed to the Secretary, Memorial Hospital, Peterborough.

PERTH. COUNTY AND CITY OF PERTH GENERAL HOSPITALS. The following House Officer posts will fall vacant on 1st February, 1958 :—

Bridge of Earn Hospital

* 1 SENIOR HOUSE SURGEON (Fracture and Orthopædic Unit).
* 2 HOUSE SURGEONS (Fracture and Orthopædic Unit).
* 3 HOUSE SURGEONS (general surgical wards).
† 1 HOUSE SURGEON or SENIOR HOUSE SURGEON (E.N.T. ward).
2 HOUSE PHYSICIANS (general medical wards).

Notes :

1. Senior House Officer posts are tenable for 12 months and Junior House Officer posts for 6 months.
2. All Junior House Officer posts are recognised for pre-registration hospital service.
3. Posts marked * are recognised by the Royal College of Surgeons under the regulations for the F.R.C.S.
4. Post marked † is recognised under the regulations for the D.L.O.

Applications, giving age, qualifications, experience and names of 2 referees, should be sent to the Group Medical Superintendent, Perth Royal Infirmary, Perth.

PLYMOUTH. SCOTT ISOLATION HOSPITAL. House PHYSICIAN (resident, Male), post vacant 7th February, 1958. Recognised pre-registration post which offers excellent experience.

Applications should be sent to the Group Secretary, Plymouth Special Hospital Management Committee, 8, Nelson-gardens, Stoke, Plymouth, Devon.

PLYMOUTH. THE SCOTT ISOLATION HOSPITAL. PLYMOUTH SPECIAL HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER from registered medical practitioners who have preferably been qualified for 1 year, and have had previous hospital experience. The applicant should preferably be able to drive a car. The duties, in 2 departments, will be chiefly in connection with infectious and venereal diseases, the former including a substantial proportion of cases in children. The varied clinical work, including acute medical cases, provides valuable experience particularly to those reading for a higher medical degree, or contemplating general practice. The appointment will be for 1 year, vacant immediately. The post is non-resident, but the successful candidate will be required to live near the Hospital and be on the telephone.

Applications, together with copies of 2 recent testimonials, should be sent to the Group Secretary, Plymouth Special Hospital Management Committee, 8, Nelson-gardens, Stoke, Plymouth, as soon as possible.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL. SENIOR HOUSE OFFICER in Anæsthetics, vacant 1st April, 1958. Recognised for the D.A., and F.F.A. R.C.S.

Applications, giving age, nationality and experience, with names of 3 referees, to be sent to the Group Secretary, 7, Nelson-gardens, Stoke, Devonport.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL, FREEDOM FIELDS. Central Casualty Department SENIOR HOUSE OFFICER in Casualty, vacancies 1st February, 1st April, 1958. Recognised for the F.R.C.S.

Applications, stating names of 3 referees, to be sent to the Group Secretary.

PORTSMOUTH AND ISLE OF WIGHT AREA PATHOLOGICAL SERVICE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the post of REGISTRAR in Pathology. The successful candidate will be expected to do a tour of duty in the departments of bacteriology, hæmatology, histology and biochemistry at the Central Laboratory, and may also be required to work in any of the laboratories covered by the Service. The Laboratory is recognised for the Diploma of Pathology. Vacant 1st April, 1958.

Forms of application may be obtained from the Group Secretary, Portsmouth Group Hospital Management Committee, Saint Mary's Hospital, Milton, Portsmouth, which should be returned to him, duly completed, on or before 3rd February, 1958. Canvassing will disqualify. Candidates may visit the Central Laboratory, Milton-road, Portsmouth, by arrangement with the Senior Pathologist.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE.

(1) **Saint Mary's Hospital**

(*a*) SENIOR HOUSE OFFICER (medical). Vacant now.
(*b*) PÆDIATRIC HOUSE PHYSICIAN. Vacant 8th February, 1958.
(*c*) HOUSE SURGEON (pre-registration). Vacant 30th January, 1958, 1st February, 1958, 9th February, 1958, 11th February, 1958.
(*d*) HOUSE PHYSICIAN (pre-registration). Vacant 31st January, 1958, 12th February, 1958.

(2) **Royal Portsmouth Hospital**

(*a*) PÆDIATRIC MEDICAL HOUSE PHYSICIAN. Vacant 1st February, 1958.
(*b*) ORTHOPÆDIC SENIOR HOUSE OFFICER. Vacant now.
(*c*) HOUSE OFFICER (orthopædic) (pre-registration). Vacant now.

(3) **Queen Alexandra Hospital**

(*a*) SENIOR HOUSE OFFICER (medical and dermatology). Vacant 29th January, 1958.
(*b*) HOUSE PHYSICIAN (pre-registration). Vacant 1st February, 1958.
(*c*) HOUSE SURGEON (pre-registration). Vacant 12th February, 1958.

Applications, stating age, experience and qualifications, together with the names of 2 referees, should be forwarded as soon as possible to E. H. HURST.

St. Mary's Hospital, Milton-road, Portsmouth.

POOLE GENERAL HOSPITAL, Poole, Dorset. (330 Beds.) BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT ANÆSTHETIC REGISTRAR. The post, which became vacant on 21st December, 1957, and is tenable for 1 year in the first instance, is recognised for the D.A. and the F.F.A. R.C.S. A furnished flat is available.

Forms of application obtainable from the Group Secretary, Hospital Management Committee Office, Royal Victoria Hospital, Gloucester-road, Boscombe, should be returned to him, duly completed, not later than Wednesday, 22nd January, 1958.

READING COMBINED HOSPITALS. Area Department OF OBSTETRICS AND GYNÆCOLOGY. (100 Beds.) Applications are invited from registered medical practitioners for the resident post of HOUSE SURGEON to the above Department. The appointment, which is vacant on the 19th February, 1958, is for 1 year, with 6 months' gynæcology at the Royal Berkshire Hospital, and 6 months in the maternity unit at Battle Hospital. Both appointments are recognised for the Diplomas of the Royal College of Obstetricians and Gynæcologists.

Write, stating age and qualifications with dates, nationality and present appointment, with copy of 1 recent testimonial, to Secretary, Royal Berkshire Hospital, Reading.

ROCHDALE AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT CLINICAL PATHOLOGIST (Senior House Officer grade) in the Department of Pathology of the Rochdale Group of hospitals. A new Department of Pathology is now being completed and will be opened early this year. The duties will consist mainly of clinical pathology, also general and emergency work and supervision of the blood banks. Previous pathology experience is not essential.

Applications, giving usual particulars and names and addresses of 2 referees, to Group Secretary, Central Offices, Birch Hill Hospital, Rochdale, Lancashire, at once.

ROCHFORD, ESSEX. GENERAL HOSPITAL. (622 Beds.) SENIOR HOUSE OFFICER required for Geriatric Unit at the above Hospital. Post vacant approximately 1st March, 1958. A wide range of facilities are available at the Hospital for the investigation, treatment and rehabilitation of acute and chronic cases.

Applications, stating age, &c., to be sent to the Secretary at the above Hospital as soon as possible.

ROMFORD, ESSEX. RUSH GREEN HOSPITAL. SENIOR HOUSE OFFICER (Male or Female) required from 5th February, 1958. Duties include work in general medicine and in the regional poliomyelitis unit (30 Beds) where excellent experience of modern methods can be obtained. Resident post.

Applications to the Medical Superintendent.

ROMFORD, ESSEX. RUSH GREEN HOSPITAL. (301 Beds.) RESIDENT HOUSE PHYSICIAN (Male or Female) required from 7th February, 1958. This Hospital provides for acute medical, surgical and infectious patients. The post, which is also open to pre-registration candidates, offers good opportunities for gaining experience in both general medicine and fevers.

Applications should be addressed immediately to the Medical Superintendent, stating also names of 2 referees.

ROMFORD. RUSH GREEN HOSPITAL. (301 Beds.) RESIDENT SENIOR HOUSE SURGEON required from 11th February, 1958. Recognised for the F.R.C.S. Good experience in busy surgical unit.

Applications should be forwarded immediately to Medical Superintendent, stating also names of 2 referees.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) RESIDENT HOUSE SURGEON required from 24th January, 1958. Open to either pre-registration applicants or to fully registered practitioners.

Apply immediately to Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital.

ROMFORD, ESSEX. OLDCHURCH HOSPITAL. (722 Beds.) SENIOR HOUSE OFFICER (resident or non-resident) required for duties in the Casualty Department. Available for Male or Female applicants. This is a large general hospital with specialised departments dealing with all types of acute medical and surgical cases. The post affords good opportunity for gaining tuition and experience.

Applications should be forwarded immediately to the Group Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

ROTHERHAM. MOORGATE GENERAL HOSPITAL. (342 Beds, 38 Cots.) RESIDENT HOUSE PHYSICIAN.

Applications to the Secretary, Hospital Management Committee, "Fern Bank," Doncaster-road, Rotherham.

ROTHERHAM HOSPITAL AND ROSEHILL HOSPITAL ANNEXE. (161 Beds and 26 Beds.) RESIDENT HOUSE PHYSICIAN.

Applications to the Secretary, Hospital Management Committee, "Fern Bank," Doncaster-road, Rotherham.

ROTHERHAM HOSPITAL AND ROSEHILL HOSPITAL ANNEXE. (161 Beds and 26 Beds.) RESIDENT HOUSE SURGEON (casualty and surgery).

Applications to the Secretary, Hospital Management Committee, "Fern Bank," Doncaster-road, Rotherham.

ROTHERHAM HOSPITAL, Doncaster Gate (161 Beds). MOORGATE GENERAL HOSPITAL, ROTHERHAM (342 Beds, 38 Cots). RESIDENT HOUSE SURGEON (casualty, E.N.T. and Eye Departments).

Applications to the Secretary, Hospital Management Committee, "Fern Bank," Doncaster-road, Rotherham.

RUGBY. HOSPITAL OF ST. CROSS. (152 Beds.) CASUALTY AND ACCIDENT OFFICER (Junior Hospital Medical Officer), resident. Vacant now. Recognised F.R.C.S. Duties include orthopædic surgery.

Applications to Hospital Secretary.

SALFORD, 6. HOPE HOSPITAL. Salford Hospital MANAGEMENT COMMITTEE. Applications are invited for the post of SECOND RESIDENT CLINICAL PATHOLOGIST, Senior House Officer grade, in the Group Laboratory at Hope Hospital, Salford, which becomes vacant at the end of January, 1958. Post recognised for the Diploma in Pathology.

Applications, together with details of age, qualifications and the names and addresses of 2 referees, should be forwarded to the Hospital Secretary.

SALFORD ROYAL HOSPITAL. Salford Hospital MANAGEMENT COMMITTEE. Applications invited for the post of SENIOR HOUSE OFFICER (Orthopædic and Casualty Departments), resident. Post vacant February, 1958. Gives opportunity for emergency surgery. Applications also invited for the pre-registration post of HOUSE SURGEON to the Genito-urinary Department at the above Hospital.

Applications, with copies of 3 recent testimonials, to the Secretary, Salford Royal Hospital, Salford, 3.

SALISBURY GENERAL HOSPITAL. Applications are invited for the appointment of RESIDENT HOUSE SURGEON for a period of 6 months. Post open to pre-registration candidates.

Apply, giving names and addresses of 2 referees, to Group Secretary, Salisbury Group Hospital Management Committee, Odstock Hospital, Salisbury.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. REGISTRAR in Dermatology at the Royal Infirmary of Edinburgh.

Apply, giving particulars of age, qualifications and previous experience, together with the names of 2 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, 3, by 8th February, 1958.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance :—

REGISTRAR in Anæsthetics based at the Western Infirmary, Glasgow.

REGISTRAR in E.N.T. Surgery based at the Glasgow Royal Infirmary with duties possibly at Law Hospital, Carluke.

REGISTRAR in Pathology based at the Victoria Infirmary, Glasgow.

REGISTRAR in Radiodiagnosis based at the Royal Infirmary, Glasgow.

REGISTRAR in Dermatology based at Stobhill General Hospital, Glasgow.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 1st February, 1958.

SHOREHAM-BY-SEA, SUSSEX. SOUTHLANDS HOSPITAL. (411 Beds.) Locum SURGICAL REGISTRAR required from 17th February, 1958, for 3 months.

Apply Hospital Secretary, Southlands Hospital, as soon as possible. A. V. OAKTON, Group Secretary,
Worthing Group Hospital Management Committee.
129, Brighton-road, Worthing, Sussex.

SHREWSBURY. ROYAL SALOP INFIRMARY/COPTHORNE HOSPITAL. (500 Beds.) HOUSE SURGEON. Vacant mid-January. Pre-registration candidates eligible. Recognised for the F.R.C.S.

Applications, with copy testimonials, to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SHEFFIELD, 5. CITY GENERAL HOSPITAL. Applications are invited for the resident (pre-registration) post of HOUSE SURGEON in Orthopædics, which becomes vacant on 15th January, 1958.

Applications, giving full details of age, nationality, qualifications, present and previous appointments with dates, and the names of 2 persons to whom reference may be made, should be forwarded to the Group Secretary, Sheffield No. 1 Hospital Management Committee, Nether Edge Hospital, Sheffield, 11.

SHEFFIELD. MIDDLEWOOD HOSPITAL. (2089 Beds—Recognised for D.P.M.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time REGISTRAR (Psychiatry) required immediately. Single accommodation available. Facilities for postgraduate study in conjunction with Sheffield University available.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 27th January, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS BOARD OF GOVERNORS and SHEFFIELD REGIONAL HOSPITAL BOARD. Reciprocal training scheme for Senior Registrars. Whole-time SENIOR REGISTRAR in E.N.T. Surgery required with initial tenure of appointment at the Royal Infirmary and Children's Hospital, Sheffield. Appointment for 1 year in the first instance and renewable annually thereafter. Successful candidate will be transferred to the Royal Infirmary, Leicester, for the second phase of the appointment, in accordance with the arrangements under the reciprocal training scheme. Renewal of appointment and transfer will be subject to satisfactory work and progress.

Applications, with the names of 3 referees, to the Chief Administrative Officer, The United Sheffield Hospitals, Weststreet, Sheffield, 1, not later than 21st January, 1958.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. THE CHILDREN'S HOSPITAL. Applications invited for the vacant post of SENIOR HOUSE OFFICER or HOUSE OFFICER (resident) in Surgery, grade according to experience.

Applications, stating age, qualifications and experience, with the names of 3 referees or copy testimonials, to the Superintendent, Children's Hospital, Western Bank, Sheffield, 10, immediately.

SHEFFIELD. WHARNCLIFFE HOSPITAL. (129 Beds.) HOUSE OFFICER (surgery) resident, pre-registration post, vacant from 15th January, 1958.

Applications, with copy testimonials, to Group Secretary, Sheffield No. 2 Hospital Management Committee, Middlewood Hospital, Sheffield, 6.

SHEFFIELD, 10. LODGE MOOR HOSPITAL. (467 Beds.) SHEFFIELD NO. 3 HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of RESIDENT SENIOR HOUSE OFFICER in Infectious Diseases, commencing late March, 1958. Candidates should have held a resident appointment in a hospital. Salary £819 10s. p.a. subject to a deduction of £150 p.a. for residential emoluments. The appointment is normally for 1 year, subject to 1 month's notice on either side.

Applications, stating age, qualifications, &c., to the Group Secretary, Sheffield No. 3 Hospital Management Committee, Lodge Moor Hospital, Sheffield, 10.

SLOUGH, BUCKINGHAMSHIRE. UPTON HOSPITAL. HOUSE PHYSICIAN required for post vacant 12th February. Pre-registration post offering considerable experience in general acute medical work.

Applications, with names of 2 referees, to Secretary by 22nd January.

SOUTHALL, MIDDLESEX. ST. BERNARD'S HOSPITAL FOR NERVOUS AND MENTAL DISORDERS. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required at above Hospital for duty on or after 1st April. Hospital undertakes all modern psychiatric treatments both physical and psychotherapeutic, and the medical staff conduct several psychiatric outpatient clinics. Hospital may be visited by direct appointment.

Application forms obtainable from and returnable to the Group Secretary, St. Bernard's Hospital Management Committee, St. Bernard's Hospital, Southall, Middlesex, by 1st February, 1958.

SOUTHAMPTON GENERAL HOSPITAL. (469 Beds. Recognised for the membership and diploma examinations of the R.C.O.G.) RESIDENT HOUSE SURGEON (pre-registration) to the Gynæcological and Obstetric Unit required mid-February.

Applications, with copies of recent testimonials, should be forwarded as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON GENERAL HOSPITAL. (469 Beds.) RESIDENT HOUSE PHYSICIAN required in February. Pre-registration candidates eligible.

Applications, with copies of testimonials, should be forwarded as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (274 Beds.) Recognised for F.R.C.S. CASUALTY OFFICER (Senior House Officer grading) required.

Applications, with copies of testimonials, to be submitted as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (274 Beds.) RESIDENT HOUSE SURGEON required. Pre-registration candidates eligible.

Applications, with copies of recent testimonials, should be forwarded to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (274 Beds. Recognised for F.R.C.S.) ORTHOPÆDIC HOUSE SURGEON (post recognised for pre-registration service and tenable for 6 months). The Hospital is the centre to which all trauma from a large industrial town and port is directed, thus providing excellent experience in the treatment of traumatic conditions; patients with orthopædic conditions are drawn from a wide area.

Applications, with copies of testimonials, should be sent as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL (274 Beds) and SOUTHAMPTON GENERAL HOSPITAL (469 Beds). SENIOR HOUSE OFFICER (E.N.T.) required in February. This post is recognised for the F.R.C.S. (Eng.) and D.L.O. examinations and provides experience in all branches of E.N.T. work. The Group includes a diagnostic and distributing hearing-aid centre.

Applications, with copies of recent testimonials, should be forwarded as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTH-WESTERN REGIONAL HOSPITAL BOARD. (Joint appointment with the United Bristol Hospitals.) Applications are invited by the above Boards for the joint appointment of REGISTRAR in Anæsthetics with duties mainly at the Royal Devon and Exeter Hospital, Exeter. The appointment, which is non-resident, will be held for 1 year in the first instance and renewable for a further year.

Applications, stating date of birth, qualifications and experience, together with the names and addresses of 2 referees, should be sent to the Secretary of the Regional Hospital Board, 27, Tyndalls Park-road, Bristol, 8, not later than 30th January, 1958.

SOUTHEND GENERAL HOSPITAL. Applications are invited for the post of TEMPORARY CASUALTY OFFICER (Registrar). Duties chiefly in Casualty Department, which is under the supervision of the Consultant in Orthopædic Surgery. Opportunities for work in fracture clinics in association with work of Orthopædic Department. The post is recognised for the F.R.C.S. if held for 6 months.

Applications, stating age, qualifications and experience, to be sent to the undersigned as soon as possible.
J. C. FIELD, Secretary.

SOUTHEND. GENERAL HOSPITAL. Applications are invited from registered or provisionally registered practitioners for the post of RESIDENT HOUSE SURGEON, vacant 9th March, 1958.

Applications, stating age, qualifications, &c. (1 testimonial sufficient from pre-registration candidates seeking first appointment) to reach the Secretary not later than 30th January, 1958.

SOUTHEND. GENERAL HOSPITAL. (262 Beds.) Temporary SENIOR SURGICAL HOUSE OFFICER required for approximately 3 months, but probably longer.

Applications should be sent to the Secretary at the Hospital by 31st January, 1958.

SOUTHEND-ON-SEA. GENERAL HOSPITAL. Applications are invited from fully registered practitioners for the post of RESIDENT HOUSE PHYSICIAN (House Officer grade). Post vacant 5th March, 1958. Appointment primarily to Pædiatric Department, with duties in Cardiological and Skin Departments. Post recognised for D.C.H.

Applications, stating age, qualifications and previous experience, with copies of recent testimonials, should reach the Secretary at the Hospital by 30th January, 1958.

ST. ALBANS CITY HOSPITAL. (384 Beds.) North West METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time GYNÆCOLOGICAL AND OBSTETRIC REGISTRAR required. Post vacant 16th February, 1958. Hospital may be visited by direct appointment.

Application forms obtainable from and returnable to Secretary, Mid Herts Group Hospital Management Committee, Bleak House, Catherine-street, St. Albans, Herts, by 28th January, 1958.

STARCROSS, DEVON. THE ROYAL WESTERN COUNTIES INSTITUTION HOSPITAL GROUP. Applications invited from registered medical practitioners (locally resident) for part-time appointment of PHYSICIAN (10h) at Franklyn Home, Broadway, Exeter. Equivalent 1 half-day weekly.

Applications to Medical Superintendent, Executive Offices, Starcross.

STIRLING AND CLACKMANNAN HOSPITALS BOARD OF MANAGEMENT. The following vacancies exist for Resident House Officers from 1st February, 1958:—

Stirling Royal Infirmary

2 HOUSE SURGEONS (1 general, 1 casualty).

Airthrey Castle Maternity Hospital

1 HOUSE SURGEON (obstetrics).

These are pre-registration posts.

Applications should be sent to the Group Medical Superintendent, Stirling Royal Infirmary (Stirling 1700).

STOCKTON AND THORNABY HOSPITAL, Stockton-ON-TEES. (130 Beds.) TEES-SIDE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of Locum SENIOR HOUSE OFFICER (casualty) at the above Hospital for duties to commence 20th January, 1958.

Applications, with full details, should be addressed as soon as possible to the Hospital Secretary.

STOKE-ON-TRENT. BUCKNALL HOSPITAL. (84 Infectious, 40 chest beds for children, 24 pneumoconiosis, 124 chronic sick beds.) Applications are invited for post of RESIDENT JUNIOR HOSPITAL MEDICAL OFFICER, vacant 1st February. Married accommodation available. The person appointed will be associated with all departments of the Hospital and will be required to assist at the pneumoconiosis clinic.

Detailed applications, with copy testimonials, to Physician-Superintendent, at the Hospital.

STOKE-ON-TRENT. NORTH STAFFORDSHIRE ROYAL INFIRMARY. SENIOR HOUSE OFFICER (general surgery) required. Recognised for F.R.C.S.

Detailed applications, with copy testimonials, to Hospital Secretary, North Staffordshire Royal Infirmary, Stoke-on-Trent, as soon as possible.

SULLY HOSPITAL, Sully, Glamorganshire. Regional THORACIC CENTRE. (324 Beds.) SENIOR HOUSE OFFICER (surgical) required. Experience will be gained in investigation and treatment of chest and heart conditions.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

SUTTON AND CHEAM HOSPITAL, Cotswold-road, SUTTON, SURREY. (146 Beds.) HOUSE SURGEON (pre-registration or fully registered). Post vacant 1st February.

Applications, stating age, experience and qualifications, with copies of recent testimonials and the names of 2 referees, should be sent to the Secretary at above address.

SWANSEA HOSPITAL, Swansea. (413 Beds.) Glantawe HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident post of SENIOR HOUSE OFFICER in the Surgical Unit of the above Hospital. Vacancy 4th February, 1958. The post is recognised under the F.R.C.S. (Eng.) regulations.

Applications, stating age, qualifications, and experience, together with copies of 2 recent testimonials, should be forwarded to the Secretary of the Hospital.

T. E. JONES, Group Secretary.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. HOUSE SURGEON required for post vacant 21st January. Pre-registration post.

Applications, stating age, qualifications with dates, and copies of 2 testimonials, to Secretary.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. HOUSE PHYSICIAN required for post vacant 9th March. Pre-registration post.

Applications, stating age, experience and qualifications with dates, and copies of 2 testimonials, to Secretary.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. Locum REGISTRAR required immediately until October to the Special Unit for Research in Juvenile Rheumatism at above Hospital. Post offers scope in research, pædiatrics, rheumatology or cardiology.

Applications, stating age, qualifications and experience, with copies of 2 recent testimonials, to Secretary.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. Locum HOUSE SURGEON required for 3 months commencing 17th January.

Apply, with copies of 2 recent testimonials, to Hospital Secretary.

TAUNTON AND SOMERSET HOSPITAL. Applications are invited for the post of HOUSE OFFICER (E.N.T.). Post-registration appointment, recognised for F.R.C.S. and D.L.O.

Applications, stating age, nationality and qualifications, together with the names of 2 referees, should be forwarded to the Group Secretary, Taunton Hospital Management Committee, Taunton and Somerset Hospital, Musgrove Park Branch, Taunton, Somerset.

TAUNTON AND SOMERSET HOSPITAL, Taunton, Somerset. (423 Beds.) HOUSE OFFICER (general surgery) required. Pre-registration post, recognised for F.R.C.S.

Applications, stating age, nationality and qualifications, to the Group Secretary, Taunton Hospital Management Committee, c/o Musgrove Park Hospital, Taunton, Somerset.

TORQUAY. TORBAY HOSPITAL. (166 general beds.) RESIDENT HOUSE OFFICER (surgical), Male or Female, required immediately. Post recognised for F.R.C.S. and pre-registration purposes. There is a complement of 6 Resident House Officers.

Applications, stating qualifications, nationality and age, together with copy testimonials (quoting reference F.955/84), to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

TUNBRIDGE WELLS (near). PEMBURY HOSPITAL, PEMBURY. Applications invited for appointment of SENIOR ORTHOPÆDIC HOUSE SURGEON AND CASUALTY OFFICER (Senior House Officer grade) to begin duties as soon as possible. Recognised F.R.C.S. (Eng.) and tenable for 1 year. Work includes treatment of long and short stay cases and traumatic surgery with large Outpatient and Fracture Clinics under 2 Consultants.

Apply, stating age, qualifications and experience, together with 3 testimonials, to Group Secretary, Sherwood Park, Pembury-road, Tunbridge Wells.

WAKEFIELD. STANLEY ROYD HOSPITAL. Applications invited for post of JUNIOR HOSPITAL MEDICAL OFFICER or SENIOR HOUSE OFFICER in Psychiatry. Accommodation available for a single person and may be available for a married person.

Address applications, giving full personal particulars, details of training, experience, &c., and 2 names and addresses for reference, to W. BOWRING, Group Secretary, Pinderfields General Hospital, Wakefield.

WARWICK (near). CENTRAL MENTAL HOSPITAL. (1400 Beds.) SENIOR HOUSE OFFICER. Neurosis unit, adult and child psychiatry clinics, departments of electro-encephalography, occupational therapy, psychology and social work. Recognised for D.P.M. Accommodation available. Post available mid-January.

Applications, with names and addresses of 3 referees, to Medical Superintendent.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL. (208 Beds.) Applications are invited for the post of HOUSE SURGEON at the above Hospital. This is a pre-registration post and is recognised for F.R.C.S. Salary according to the National Health Service scale.

Applications, with copies of recent testimonials, to the Administrator.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL. (208 Beds.) HOUSE PHYSICIAN required at the above Hospital. Pre-registration post. Salary in accordance with National Health Service scales.

Applications, with copies of 2 recent testimonials, to the Administrator immediately.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL. (208 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST (Senior House Officer grade) to the Watford Hospitals. Post vacant early March.

Applications, together with copies of not more than 2 recent testimonials, to the Administrator.

WATFORD. SHRODELLS HOSPITAL. (General Hospital—320 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER to the Geriatric Unit, to take up duty early in February. Modern Geriatric Unit of 180 beds. Adequate time for reading. The Hospital is within reach of London teaching classes.

Applications, together with copies of 2 testimonials, should reach the Medical Administrator as soon as possible.

WEST HARTLEPOOL. GENERAL HOSPITAL. (471 Beds.) Applications are invited for the post of SENIOR HOUSE PHYSICIAN at the above Hospital, vacant beginning of March.

Applications, stating age, nationality and qualifications with dates, and accompanied by copies of 2 testimonials, should be sent to the Group Secretary, Hartlepools Hospitals Management Committee, at the General Hospital, West Hartlepool, as soon as possible.

WESTON-SUPER-MARE GENERAL HOSPITAL. (107 Beds.) Applications are invited from registered medical practitioners for the pre-registration appointment (resident) of HOUSE SURGEON. Immediate vacancy.

Applications, stating age, qualifications, together with names and addresses of 2 referees, should be addressed to the Secretary, Weston-super-Mare Hospital Management Committee.

WHITEHAVEN HOSPITAL, CUMBERLAND. (119 Beds and Annexe of 31 Beds.) HOUSE OFFICER (obstetrical and gynæcological) (House Officer or Senior House Officer grade). Vacant beginning of February.

Detailed applications, with dates and names of 2 referees, to the Group Secretary, Workington Infirmary, Cumberland.

WORTHING HOSPITAL, Lyndhurst-road, Worthing, SUSSEX. (210 Beds—acute general.) The post of HOUSE PHYSICIAN will be vacant in February.

Applications from registered medical practitioners, stating age, qualifications, experience, nationality, and enclosing copies of 2 recent testimonials, to be forwarded to the Hospital Secretary immediately. A. V. OAKTON, Group Secretary,
Worthing Group Hospital Management Committee.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL. (315 Beds.) HOUSE SURGEON to the Senior Surgeon. Post vacant 16th February.

Applications, with copies of 2 testimonials, to the Group Secretary.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL. (315 Beds.) HOUSE SURGEON (post recognised by Royal College of Surgeons) required for general surgery with some E.N.T. duties. Approved pre-registration post. Vacant 28th February.

Applications, with copies of 2 testmonials, to Group Secretary.

WINDSOR. KING EDWARD VII HOSPITAL. House PHYSICIAN required, Male or Female, for post vacant 11th February. Pre-registration post.

Applications, stating age, qualifications with dates, nationality, and copies of 3 recent testimonials, to Secretary, as soon as possible.

WINDSOR. KING EDWARD VII HOSPITAL. Casualty OFFICER required, Senior House Officer grade. Department forms part of Accident Service of Windsor Group. Duties include House Surgeon to E.N.T. and Eye Departments. Previous experience in treatment of acute injuries desirable.

Applications, stating age, qualifications, with dates, nationality, with copies of recent testimonials, to Secretary.

WOKING AND CHERTSEY GROUP LABORATORY. Applications are invited for the post of RESIDENT CLINICAL PATHOLOGIST (Senior House Officer). The post is 1 of 2, and involves a half-share in the emergency service. Training will be available in all branches of clinical pathology. Post tenable for 1 year. Salary £819 10s. p.a. (deduction for board and lodging £150 p.a.).

Applications, stating age, qualifications, &c., together with the names of 2 referees, should be sent as soon as possible to The Director, Group Laboratory, St. Peter's Hospital, Chertsey, Surrey.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An Associated Hospital of the Birmingham University Medical School.) HOUSE OFFICER (pre-registration) E.N.T. Department, recognised for the D.L.O. and F.R.C.S. examinations. Vacant 1st March.

Apply, giving age and qualifications, with copies of 2 testimonials, to the Hospital Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An Associated Hospital of the Birmingham University Medical School.) Pre-registration HOUSE OFFICER (pædiatrics) required. Vacant 20th January, 1958.

Apply, giving age and qualifications, with copies of 2 testimonials, to the Hospital Secretary.

WOLVERHAMPTON. THE ROYAL HOSPITAL. (An Associated Hospital of the Birmingham University Medical School.) Pre-registration HOUSE OFFICERS. Vacancies in surgery occur on 23rd January, 1958.

Apply, giving age and qualifications, with copies of 2 testimonials, to the Hospital Secretary,

WREXHAM. MAELOR GENERAL HOSPITAL. (591 Beds.) Applications are invited for the posts of HOUSE SURGEON (2) at the above Hospital, to commence duties on 1st February, 1958. The appointments are recognised for the diploma of F.R.C.S. (England, Edinburgh, and Ireland) and are pre-registration posts.

Applications, stating age, nationality, qualifications and experience, with copies of 2 recent testimonials, to be sent to the Group Secretary, Maelor General Hospital, Wrexham, as soon as possible.

WREXHAM. WAR MEMORIAL HOSPITAL. (230 Beds.) Applications are invited for the posts of HOUSE SURGEON (2) at the above Hospital, to commence duties on 1st February, 1958. The appointments are recognised for the Diploma of F.R.C.S. (England and Edinburgh) and are pre-registration posts.

Applications, stating age, nationality, qualifications and experience, with copies of 2 recent testimonials, to be sent to the Group Secretary, Maelor General Hospital, Wrexham, as soon as possible.

U.S.A. ST. ELIZABETH HOSPITAL, Covington, Kentucky. (400-Bed Hospital.) Required, INTERNES. Internship approved by the American Medical Association. Rotate through services in surgery, medicine, pediatrics, obstetrics and emergency room. Starts 1st July, 1958 and ends 30th June, 1959. Salary $200 per month with maintenance.

Contact Hospital.

U.S.A. UNIVERSITY OF MINNESOTA MEDICAL CENTER. ANESTHESIOLOGY RESIDENCIES at the above Center. 2 or 3-year programme with clinical and didactic instruction in all phases of anæsthesia. Board approval. Positions starting every month.

Address, F. H. VANBERGEN, M.D., University of Minnesota Medical Center, Minneapolis 14, Minnesota.

Public Appointments

BOURNEMOUTH. COUNTY BOROUGH OF BOURNEMOUTH. Applications are invited from registered medical practitioners, holding a qualification in public health, for the superannuable appointment of DEPUTY MEDICAL OFFICER OF HEALTH AND DEPUTY PRINCIPAL SCHOOL MEDICAL OFFICER. Candidates should be experienced in general public health administration and be capable of assuming full responsibility for the Health Department in the absence of the Medical Officer of Health. The salary will be within the scale of £1415–£55 (4)–£50 (1)–£1685, plus a car allowance of £110.

Further information regarding the appointment and forms of application may be obtained from the Medical Officer of Health, Public Health Department, 17, St. Stephen's-road, Bournemouth, to whom completed applications should be returned not later than 21st January, 1958.

A. LINDSAY CLEGG, Town Clerk.

SECOND ADVERTISEMENT

WESTMINSTER CITY COUNCIL AND HOLBORN BOROUGH COUNCIL. Joint appointment of DEPUTY MEDICAL OFFICER OF HEALTH (permanent superannuable post). Salary £2050–£106–£2365 p.a. Applicants to be registered medical practitioners and to hold a registered public health qualification; age under 46 years at 1st January, 1958. The person appointed will act as Deputy Medical Officer of Health for the 2 boroughs. His services will be allocated in the proportion of 3/4ths to Westminster and 1/4th to Holborn.

Applications (marked "Deputy Medical Officer of Health"), stating age, war service, qualifications, present and past appointments, with names of 3 referees, to the Town Clerk, Westminster City Hall, Charing Cross-road, London, W.C.2, by 7th February, 1958.

Applications received in reply to the first advertisement will be reconsidered if the candidates so request.

FACTORY DOCTORS. Factories Acts, 1937 and 1948. The following appointments as Appointed Factory Doctor are vacant. Apply to Chief Inspector of Factories, 19, St. James's-square, London, S.W.1:—

District	*County*	*Latest date for receipt of applications*
WOOTTON BASSET	WILTS	1ST FEBRUARY, 1958
EASTWOOD	NOTTINGHAM	1ST FEBRUARY, 1958
BARTON-ON-HUMBER	LINCOLN	1ST FEBRUARY, 1958
STAVELEY	DERBY	1ST FEBRUARY, 1958
ANNBANK	AYR	1ST FEBRUARY, 1958

GLOUCESTERSHIRE COUNTY COUNCIL. Senior MEDICAL OFFICER, Maternal and Child Welfare. Applicants should have a wide experience of maternal and child welfare. Salary £1520–£1955, superannuable, medical examination, car driver, and should possess a motorcar.

Application forms obtainable from County Medical Officer of Health, Berkeley House, Berkeley-street, Gloucester, returnable by 1st February, 1958.

GUY H. DAVIS, Clerk of the County Council.

Shire Hall, Gloucester.

MANCHESTER. CITY OF MANCHESTER HEALTH DEPARTMENT. MEDICAL OFFICER required for duties mainly in connection with the City Council's scheme for immunisation and vaccination. Salary £1050–£1475. Medical Council "C" conditions of service.

Application forms may be obtained from the Town Clerk, Town Hall, Manchester, 2, and should be returned to him not later than 25th January, 1958.

MIDDLESEX COUNTY COUNCIL. County Health DEPARTMENT. ASSISTANT MEDICAL OFFICER (whole-time) required initially in Area 4 (Finchley and Hendon). Duties concerned with supervision of the health of mothers and young children and School Health Service. Diploma in Public Health or in Child Health, and previous Local Authority experience an advantage. Salary £1050–£50(3)–£55(5)–£1475. Established, pensionable. Prescribed conditions.

Apply, stating age, qualifications, experience, and names of 2 referees, to Area Medical Officer, Town Hall, Hendon, N.W.4, by 1st March (quote W.729TL). Canvassing disqualifies.

NAVY, ARMY AND AIR FORCE INSTITUTES. Applications are invited from general practitioners in the undernoted towns for the appointment in a part-time capacity as MEDICAL OFFICERS to this Corporation. Successful applicants would be required to examine and report on the conditions of employees of the Corporation who may be referred to them from time to time. Fees for this work will be paid on a scale agreed with the British Medical Association.

Applications, giving details of qualifications and experience, should be sent to the Chief Medical Officer, Navy, Army and Air Force Institutes, Kennington-lane, London, S.E.11, not later than 25th January, 1958.

The towns for which applications are invited are :—

BICESTER	OXFORD	HIGH WYCOMBE
WINDSOR	READING	ALDERSHOT

NOTTINGHAM. CITY OF NOTTINGHAM HEALTH SERVICES. Applications invited for appointment of ASSISTANT MEDICAL OFFICER for duties which will include maternal and child health and vaccination and immunisation. Possession of the D.P.H. an advantage. Post superannuable subject to medical examination. Salary £1050–£1475 p.a. Commencing salary according to local-government experience.

Application forms to be obtained from Medical Officer of Health, Huntingdon-street, Nottingham, and to be returned to him by 8th February, 1958. T. J. OWEN, Town Clerk.

YORKSHIRE. COUNTY COUNCIL OF THE WEST RIDING OF YORKSHIRE. Joint appointment of SENIOR ASSISTANT COUNTY MEDICAL OFFICER AND SCHOOL MEDICAL OFFICER to the Bowland, Sedbergh and Settle Rural District Councils and the West Riding County Council. Applications are invited from registered medical practitioners, men or women, for the above post. The successful applicant will be on the staff of the County Medical Officer's Department, but will work under the administrative direction of the Divisional Medical Officer and Medical Officer of Health, who is responsible for the day-to-day administration of public health matters in the Division. Duties will be mainly clinical in the School Health and Infant Welfare Services, but in addition, the person appointed will act for the Divisional Medical Officer and Medical Officer of Health in his absence, and will be appointed as Deputy Medical Officer of Health to the above constituent authorities. Candidates must have at least 3 years' experience since qualification and be in possession of the D.P.H. The present scale of salary is £1150–£1575 p.a. Travelling and subsistence allowances according to the County Council's scale are payable in addition to salary. The post is superannuable and is subject to a medical examination.

Forms of application are obtainable from the undersigned, to whom they should be returned not later than 3rd February, 1958.

J. WOOD-WILSON,
County Medical Officer.

County Hall, Wakefield.

PONTYPRIDD URBAN DISTRICT COUNCIL. GLAMORGAN COUNTY COUNCIL. Applications for the mixed appointment of Male MEDICAL OFFICER OF HEALTH for the Pontypridd Urban District and ASSISTANT MEDICAL OFFICER, Glamorgan County Council, are invited from Male medical practitioners who hold the qualifications prescribed by the Sanitary Officers (Outside London) Regulations, 1935 and 1951, and who have been registered as medical practitioners for not less than 5 years. The salary for the mixed appointment will be £1717 10s. p.a., rising by 8 annual increments to a maximum of £2078 19s. 6d. p.a.; the point of entry to be in accordance with experience. The appointment will be subject to the Local Government Superannuation Act 1937/53 and to the passing of a medical examination.

Forms of application and particulars of appointment can be obtained from the undersigned Clerk of the Pontypridd Urban District Council, to whom they should be returned on or before Saturday, 1st February, 1958, endorsed "Medical Officer of Health."

BERNARD M. MURPHY,
Clerk of the Pontypridd U.D. Council.
RICHARD JOHN,
Clerk of the Glamorgan County Council.

Municipal Buildings, Pontypridd, Glam.

SURREY COUNTY COUNCIL. Child Guidance Service. Applications are invited for the part-time post of PSYCHIATRIST to the Sutton Child Guidance Clinic for 4 sessions per week. Possession of the D.P.M. essential. Remuneration at the rate of 5 guineas per session.

Applications, stating age, qualifications and details of present and previous appointments, together with the names of 2 referees, should be sent to the County Medical Officer, County Hall, Kingston-upon-Thames, not later than 27th January, 1958.

WALSALL. COUNTY BOROUGH OF WALSALL. Applications are invited from qualified medical practitioners for the post of DEPUTY MEDICAL OFFICER OF HEALTH at a salary of £1486 p.a., rising by annual increments of £55(4)–£50(1)–£1756 p.a. Applicants must possess the D.P.H. and should be approved in connection with the ascertainment of educationally subnormal children. Commencing salary according to qualifications and experience.

Further particulars and forms of application for the appointment may be obtained from the undersigned. Closing date for applications, Monday, 10th February, 1958.

W. STALEY BROOKES, Town Clerk.

Council House, Walsall.

GOVERNMENT OF TANGANYIKA. Male Medical OFFICERS with qualifications registrable in United Kingdom required for general duties. Officers would normally be based on a hospital but must be prepared to tour and to train African staff. Professional work covers a wide field in all branches of medicine, surgery and obstetrics with unusual responsibility and scope for initiative. Ample opportunities for sport and recreation. Limited private practice is at present permitted. Appointment can be made on permanent basis with pension (non-contributory), or on short-term contract with gratuity (taxable) on satisfactory completion of service. National Health Service doctor may retain superannuation rights (up to 6 years) and receive gratuity (taxable) of 20% of aggregate salary after engagement. Salary ranges from £1284 to £2115 a year, starting-point determined by experience. 4 extra increments given for approved higher qualifications. Permanent officers are eligible to be considered at any time for promotion to higher salaried posts in Tanganyika and other territories in medical administration or, if they possess higher qualification and suitable experience, in specialist posts. Quarters generally available at rental of £30 to £78 a year according to size and type, furniture £12 to £24 a year. Free passages in both directions for officer and wife and up to cost of 1 adult fare for children. Taxation at local rates. Annual local leave permissible and generous home leave after each tour of from 30 to 36 months. Educational facilities.

Application forms from Director of Recruitment, Colonial Office, Great Smith-street, London, S.W.1 (quoting BCD. 117/8/02).

WESTERN REGION OF NIGERIA. Specialist Obste-TRICIAN required for obstetrical and gynæcological duties, including outpatient, maternity, child welfare and antenatal work in the larger provincial hospitals of the Region (which are being enlarged up to 200 Beds), and to assist in training midwives. Candidates should have registrable medical qualifications and the M.R.C.O.G. or an equivalent higher qualification with considerable experience of major surgery in their specialty, and have had at least 6 years' post-registration experience.

Appointment (1 tour of 12–24 months in the first instance) may be either :—

(*a*) on contract with gratuity (taxable) on satisfactory completion of contract at rate of £37 10s. for each completed period of 3 months' service (including leave), or

(*b*) from National Health Service, candidates retaining superannuation rights and receiving gratuity (taxable) of 20% of aggregate of salary.

Salary under (*a*) £2664 a year, and (*b*) £2220.

Quarters provided at low rental. Taxes at local rates. Annual leave permissible : generous home leave granted after each tour of 12–24 months. Free return passages for officer, wife, and children (up to 3).

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting BCD. 117/410/06).

Hospital Services: Non-Medical Appointments

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL INFIRMARY. A vacancy exists for a MEDICAL PHOTOGRAPHER in the Department of Medical Illustration. Whitley Council conditions of salary and service. £440–£20 (4)–£25 (1)–£545 p.a.

Applications, together with the names of 2 referees, to the Secretary, Manchester Royal Infirmary, Manchester, 13.

BIRMINGHAM. BLOOD TRANSFUSION SERVICE. SCIENTIFIC OFFICER. Necessary qualification B.Sc. in any biological science subject. Post offers ample opportunity for original research. Previous knowledge of blood-grouping not essential. Whitley Council pay, &c.

Apply Secretary, Regional Hospital Board, 10, Augustus-road, Birmingham, 15, by 1st February, 1958. Further information from Director, Blood Transfusion Service, 15, Ampton-road, Birmingham, 15, by appointment.

General Practice

For an ***Executive Council post*** *(England and Wales) apply on form* **E.C.16A** *obtainable from the council. Mark envelope "Vacancy."*

ISLEWORTH. Applications invited for Vacancy occasioned by death of practitioner. List at present approximately 3200. "Intermediate" area. Premises may be available. Apply on Form E.C.16A before 25th January, 1958, to The Clerk, Middlesex Executive Council, North West House, 119, Marylebone-road, London, N.W.1.

MID-DEVON. Applications are invited for a rural VACANCY (death). List at present approximately 1100 (dispensing). Applications on Form E.C.16A should reach the undersigned not later than first post, 30th January, 1958. Form E.C.16A and further details obtainable on request.

Devon and Exeter Executive Council, H. BELL, Clerk.
46, Queen-street, Exeter.

Miscellaneous

The Morgan Crucible Company Limited require a full-time Medical Officer (Male) at its Battersea works where the total strength is 3500. Industrial experience is essential and D.I.H. desirable. Salary will be in accordance with B.M.A. recommendations. The Company runs a contributory pension scheme with non-contributory life insurance. Preliminary interviews will be conducted to arrive at a short list and expenses incurred in attending these interviews will be met.

Applications should be addressed to the Staff Manager (Ww), THE MORGAN CRUCIBLE COMPANY LIMITED, Battersea Church-road, S.W.11.

Rolls-Royce, Limited. Applications are invited for the post of an additional Medical Officer at Derby. Experience in casualty work and general medicine essential. Age 26–34 years. Salary from £1600 p.a.—Applications should be made, together with details of qualifications and experience, to Consultant Medical Officer, Rolls-Royce, Derby.

MEDICAL OFFICER

required by large oil company for service initially based on London but entailing overseas tours of duty and eventually for permanent service in the Middle East. Preference will be given to bachelors under 37 with overseas experience and some knowledge of tropical work. Salary in accordance with the B.M.A. salary scale. Pension scheme.—Apply, quoting No. 646, to Box No. 1396, c/o CHARLES BARKER AND SONS LTD., Gateway House, London, E.C.4.

Oxford University Press have a vacancy for a Secretary Assistant to the Medical Editor. Salary according to age and experience.—Apply to Staff Manager, Amen House, Warwick-square, E.C.4.

Doctor's receptionist, 5 years' experience, seeks post, preferably in the Midlands.—Address No. 359, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Canada. For disposal in Eastern Canada, general practice in lovely countryside, 25 miles from University town. Good sporting facilities. British degree accepted. Very little capital required. Selling price, less than 6 months' income, includes complete heavy house furnishings with modern kitchen equipment and all office equipment. Pleasant practice for young energetic married man. Available end June.—Reply Address No. 360, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Doctors requiring applications, theses copied: Write to MANTON (WESTMINSTER) LTD., 98, Victoria-street, S.W.1 (VIC 0141), who are specialists.

"Pregnancy Diagnosis by the Xenopus Method", 24-hour service. Send specimens of urine and £2 2s. fee. Hæmatology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

Microscopes. Highest prices paid for good modern types. Send or bring your equipment for valuation.—WALLACE HEATON LTD., 127, New Bond-street, W.1.

Hypnotism. Will all doctors interested in this subject for Medical purposes please write to the Secretary, British Society of Medical Hypnotists, 126, Harley-street, W.1.

Direct-writing (Philips) Electrocardiogram for sale.—Address, No. 362, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

West End. Use of Consulting-room and diagnostic radiography, electrocardiography, &c. Now available.—Address No. 361, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Watson Service Microscope, excellent condition. Objectives ⅔, ⅙, 1/12 (oil immersion). Eyepieces 10×, 15×. £30.—Phone Polden, Elmbridge 5371, Extension 1.

Doctors' Houses in New Town. Interested parties apply to Thomas Bates & Son Limited, The Old Brickworks, Harold Wood, Essex, developers of large new Estate, Stanford-le-Hope, Essex. Several thousand houses ultimately to be built, 400 now in course of erection.

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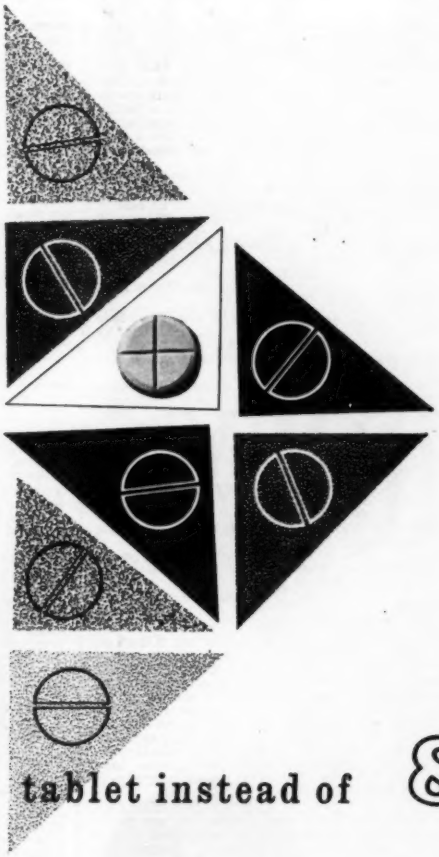

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